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# Effect of Tetraethyl Lead and Restricted Food Intake on Locomotor Activity in the Rat[1]

JAMES CRAIG SCHMIDT AND DONALD A. CZECH[2]

*Department of Psychology, Marquette University, Milwaukee, WI 53233*

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SCHMIDT, J. C. AND D. A. CZECH. *Effect of tetraethyl lead and restricted food intake on locomotor activity in the rat.* PHARMAC. BIOCHEM. BEHAV. 7(6) 489–492, 1977. – The effect of tetraethyl lead (TEL) and restricted food intake on spontaneous locomotor activity in male albino rats was investigated. Forty animals were injected intraperitoneally with 4, 7, 10 or 13 mg/kg body weight of TEL in peanut oil, or a peanut oil placebo. Forty additional animals were food yoked to lead treated animals as a control procedure to hold food intake constant between lead treated and lead free animals. A comparison of pre- and posttreatment measures revealed significant decreases in food intake and increases in activity levels at dosages of 7, 10 and 13 mg/kg of TEL. In addition, food intake and activity were significantly correlated in both lead treated and yoked groups. The issue of factors associated with reduced food intake playing a role in observed activity level increases was raised.

Tetraethyl lead  Locomotor activity  Food intake  Lead poisoning  Activity  Consummatory behavior  Hyperactivity

BEHAVIOR patterns frequently described in conjunction with excessive exposure to lead include lethargy, ataxia, seizure-like convulsions, aggressiveness, increased reactivity to stimuli, and changes in locomotor activity [1, 7, 8, 10, 15]. The last of these behaviors has generated particular interest, due in part to concern with a possible link between a high body lead burden and the widespread childhood behavior disorder referred to as hyperactivity, a term used to describe a rather complex syndrome characterized in part by high levels of motor activity [5]. Several systematic studies have reported heightened activity in conjunction with both experimentally induced [9, 11, 12] and accidental [1,6] lead poisoning with inorganic lead compounds. Studies involving systematic measures of locomotor activity following exposure to organolead compounds are, on the other hand, conspicuously absent from the literature, although hyperactivity has been noted [3, 7, 13]. Preliminary data from our laboratory also suggest that adult male rats are more active following exposure to an organolead compound, tetraethyl lead (TEL).

In a related area of inquiry, Czech *et al.* [4] reported that intraperitoneal and intragastric administration of TEL to rats at dosage levels of 7, 10 and 13 mg/kg of body weight is followed by a significant reduction of both food and water consumption. Further, locomotor activity in the rat has been reported to increase following food deprivation [2,14]. Conjointly, these two findings point out the necessity of considering food intake behavior in investigations into the possible effects of lead on locomotor activity.

The present experiment was undertaken to examine the possible effect of TEL on locomotor activity in the rat, using a yoking procedure to control for potential confounding by changes in food intake.

## METHOD

### *Animals*

Eighty male Sprague-Dawley rats (Holtzman) were used, ranging in age from 52–58 days upon arrival at the laboratory and weighing 203–245 g. They were housed individually in suspended wire mesh cages and maintained on a 12 hr light-dark cycle (0600–1800 hr) in an air conditioned room. Ground food (Purina lab chow) in nonspill cups and tap water were available ad lib, except that amount of food was regulated for the animals in yoked groups during testing.

### *Apparatus*

Locomotor activity was measured with a stabilimeter platform (Lafayette Instrument Co., Model 86010) at a gain setting of 5 in a separate air conditioned room with approximately 78 db of white noise (Grason-Stadler, Model 901A) present during testing.

### *Procedure*

Upon arrival at the laboratory, all animals were placed in cages and allowed 3 days for acclimation; no measures were taken during this time. Following this acclimation period, food intake to the nearest 0.5 g and body weight to the nearest gram were recorded daily. Activity counts for each rat were recorded daily during a single 5-min test session in

[1] This report is based on an MA thesis submitted to Marquette University by J. C. Schmidt.
[2] Requests for reprints should be sent to D. A. Czech, Department of Psychology, Marquette University, Milwaukee, WI 53233.

the stabilimeter throughout the experimental period. Running order of animals was randomized to avoid possible confounding by daily activity patterns.

A pretreatment experimental period, following acclimation, spanned 6 days and was partitioned as follows. Days 1–3 were designated as an habituation period (HAB) during which the animals were acclimated to the stabilimeter in a daily 5-min session. Activity counts obtained on Days 4–6 provided a pretreatment baseline measure (PRE) and were used for assignment of animals, using a randomized blocking procedure, to 10 treatment groups of 8 animals each.

Animals in four of the 10 treatment groups were given an intraperitoneal injection of 4, 7, 10 or 13 mg/kg body weight of TEL in peanut oil. Lead concentration was 2 mg/ml of peanut oil (w/v). Animals in a fifth group received a placebo injection of 1 ml of peanut oil. Collectively, these five groups were designated the lead treated groups. The remaining five treatment groups constituted the yoked groups, and were treated in the following manner. One of the yoked groups received 1 ml of peanut oil and the remaining four groups were given injections of peanut oil equivalent in volume to the quantity given to the lead treated groups. Animals in the five yoked groups were then individually food yoked to animals in the five lead treated groups. Food intake, in g/100 g of body weight, of a lead treated rat on any given day was used to determine the portion of food (also relative to body weight) to be given to its yoked counterpart. Thus, food consumption of the yoked member of a pair was limited to that of its lead treated mate, with the yoked groups lagging the lead treated groups by one day. The posttreatment period was divided into two blocks of 3 days each (Days 7–9 and 10–12 for the lead treated groups, and Days 8–10 and 11–13 for the yoked groups) which were designated as POST–1 and POST–2, respectively. Mean activity counts and food intake (g food/100 g body weight) were obtained for each rat over the successive blocks of days, thereby providing means for the HAB, PRE, POST–1 and POST-2 periods.

In order to facilitate data collection with a relatively large number of subjects, two replications of 40 animals each were run in succession, spaced approximately 2 weeks apart, with one-half of the animals from each group being run in each replication.

## RESULTS AND DISCUSSION

Mean food intake, expressed as g/100 g of body weight, for the lead treated groups, is shown in Fig. 1, each mean representing a block of three days. A repeated measures analysis of variance revealed significant changes in food intake as a function of dosage level, $F(4,30) = 5.25$, $p<0.003$, blocks of days, $F(3,90) = 110.05$, $p<0.001$, and replications, $F(1,30) = 18.61$, $p<0.001$. Significant first order interactions were obtained for dosage × blocks of days, $F(12,90) = 7.29$, $p<0.001$, and replications × blocks of days, $F(3,90) = 4.05$, $p<0.01$. Although the two replications were distinctly different in amounts of food intake, and the difference between replications increased across blocks of days, the replication factor did not interact significantly with the dosage factor; it was, therefore, not considered further in analysis and interpretation of the data.

Inspection of Fig. 1 reveals large decrements in food

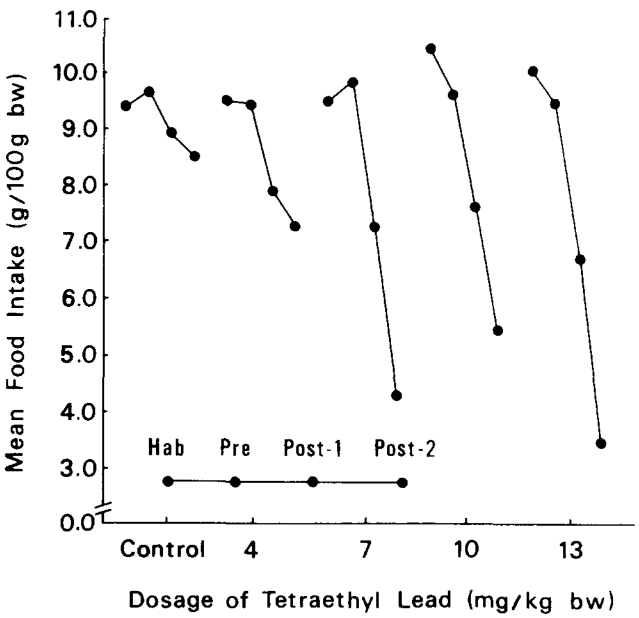


FIG. 1. Mean food intake across pre- and posttreatment periods for control and lead treated groups. Each mean represents a block of 3 days.

intake for the lead treated groups across the PRE, POST–1, and POST–2 periods, especially at the higher dosage levels. To make individual comparisons among means, Duncan's multiple range tests were used. Significant differences were noted between the PRE and POST–2 periods at dosage levels of 7, 10 and 13 mg/kg (all $p<0.001$), between PRE and POST–1 periods at 7 and 13 mg/kg (both $p<0.05$), and between POST–1 and POST–2 periods at 7 and 13 mg/kg ($p<0.05$ and $p<0.01$, respectively). These results are consistent with the finding of Czech *et al.* [4] that TEL exposure leads to reduction of ad lib food intake in the male rat at dosages of 7, 10 and 13 mg/kg of body weight. Mean body weight and food intake for lead treated groups are also presented separately in Table 1.

Lead treated vs. yoked (LT–Y) was included as a factor in the analysis of activity scores, which necessitated using a separate label, stratum, to designate a given treatment level. In order to retain an identification with dosage levels of the lead treated groups, the levels of stratification were designated as 0 (control), 4, 7, 10 and 13.

The analysis of variance revealed significant changes in activity as a function of blocks of days, $F(3,160) = 29.76$, $p<0.001$, and strata × blocks of days, $F(12,160) = 2.73$, $p<0.003$. The factors of LT–Y, LT–Y × strata, LT–Y × blocks of days, and LT–Y × blocks of days × strata were not significant. Thus, there was no evidence to indicate that the lead treated groups behaved differently from the yoked groups in amount of locomotor activity.

Mean activity counts across blocks of days for each stratum for lead treated and yoked groups, both separately and combined, are shown in Fig. 2. Duncan's multiple range tests applied to the combined LT–Y means indicated that activity increased significantly between PRE and POST–2 at strata 4, 7, 10 and 13 ($p<0.05$ at strata 4, all others $p<0.001$). In addition, comparisons made between POST–1 and POST–2 showed significant increases in activity at strata 7, 10 and 13 (all $p<0.001$).

TABLE 1

MEAN BODY WEIGHTS (UPPER) AND FOOD INTAKES (LOWER) IN GRAMS FOR LEAD TREATED GROUPS*

| Dosage mg/kg | Hab | Experimental Period Pre | Post-1 | Post-2 |
|---|---|---|---|---|
| Control | 253 (29.8) | 266 (17.4) | 285 (22.9) | 297 (28.1) |
| 4 | 243 (13.6) | 264 (13.8) | 273 (24.1) | 274 (32.0) |
| 7 | 245 (13.7) | 267 (15.1) | 277 (21.4) | 254 (27.4) |
| 10 | 245 (15.3) | 269 (18.3) | 280 (24.1) | 269 (40.1) |
| 13 | 239 (13.3) | 262 (14.0) | 270 (17.8) | 243 (28.6) |
| Control | 23.5 (5.6) | 26.0 (10.2) | 25.5 (3.2) | 25.5 (5.6) |
| 4 | 23.0 (2.9) | 25.0 (3.0) | 22.0 (5.4) | 20.5 (5.6) |
| 7 | 23.5 (2.8) | 26.5 (4.2) | 20.5 (7.1) | 11.0 (6.1) |
| 10 | 26.0 (5.2) | 26.0 (3.5) | 22.0 (6.8) | 15.5 (10.8) |
| 13 | 24.0 (2.7) | 25.0 (2.8) | 18.5 (7.0) | 9.0 (7.2) |

*SE in parenthesis.

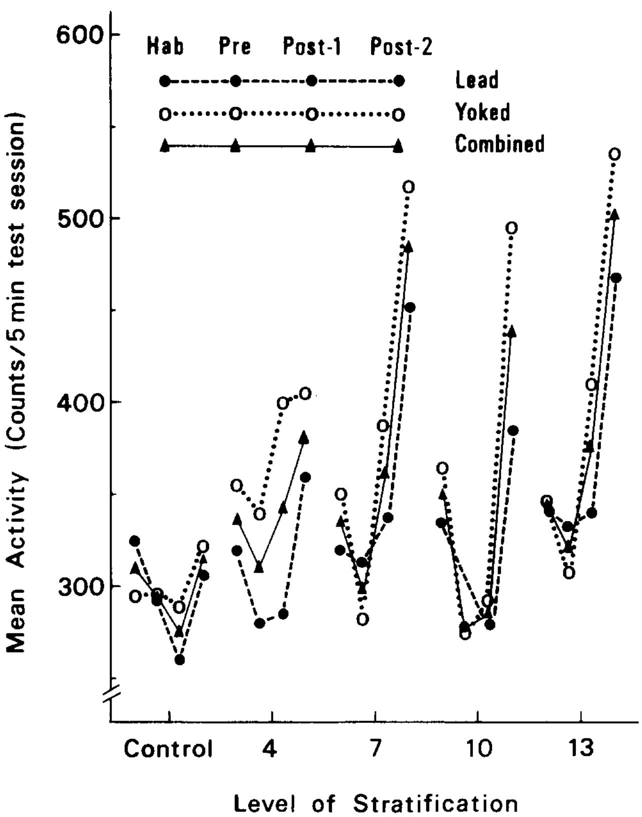


FIG. 2. Mean activity counts across pre- and posttreatment periods for the lead treated and yoked groups separately, and for the combined lead treated-yoked groups. Each mean represents a block of 3 days.

To determine the magnitude of the relationship between activity and food intake for yoked animals, a Pearson r was calculated for the PRE, POST–1 and POST–2 periods ($r(13) = -0.90, p < 0.001$). In turn, a regression equation was calculated, and used to predict activity scores from mean food intake for the lead treated groups. The ratio of the variance for the predicted to observed activity scores (ratio = 0.78) gave additional evidence of the strong relationship between food intake and activity level. As expected, food intake was found to be significantly correlated with activity in the lead treated groups as well ($r(13) = -0.88, p < 0.001$).

In view of these findings, it is tempting to speculate that the heightened activity observed might have been mediated, at least in part, by factors associated with reduced food intake. For example, Teghtsoonian and Campbell [14] offered evidence that increased activity during food deprivation in rats resulted from lowered response threshold to environmental stimulus change. However, there is no evidence, to our knowledge, to indicate how forced food deprivation and lead-induced hypophagia might be related as conditions of deprivation.

In summary, the present study demonstrates that exposure to an organolead compound, TEL, can lead to heightened locomotor activity in male rats. In addition, it raises the question of whether changes in consummatory behavior might partially account for this effect. It would be of interest to know if shifts in activity levels following lead exposure in animals could be modified by direct experimental manipulation of the intragastric environment as, for example, by forced feeding of lead treated animals. From another point of reference, the manipulation of environmental stimuli could reveal an altered degree of reactivity in TEL intoxicated rats.

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