Pharmacology Biochemistry & Behavior, Vol. 6, pp. 243–244.

BRIEF COMMUNICATION

Phenobarbital Drinking Curves After Varied Water Deprivation

HANS SCHMIDT JR. AND THOMAS BUTZER

Department of Psychology, Xavier University, Cincinnati, OH 45207

(Received 4 June 1976)

SCHMIDT, H., JR. AND T. BUTZER. *Phenobarbital drinking curves after varied water deprivation.* PHARMAC. BIOCHEM. BEHAV. 6(2) 243–244, 1977. – The phenobarbital dose-drinking response curves were obtained for 11½ and 23½ hr of water deprivation in rats. The results indicated that the same quadratic curve was found in both cases displaced as a function of degree of deprivation. These results are explicable by regarding phenobarbital as an adequate stimulus for drinking or by disinhibiting drinking if level of inhibition is not directly concerned with regulation of water ingestion per se. The response to phenobarbital upon the days following injection is similar for both degrees of deprivation investigated.

Phenobarbital Water deprivation Thirst

BARBITURATE drinking curves have been obtained which reliably demonstrate a quadratic function of approximately the form $Y = A+BX-CX^2$ [5,6]. However, these findings are from 23½ hr water deprived rats exclusively. The obvious variable of hours of deprivation has not been investigated. The only data related to the magnitude of deprivation is the result of Schmidt [4] for stomach loading with water. It was observed that 40 mg/kg phenobarbital facilitated drinking to a similar absolute volume after a 5% (volume/body weight) stomach load of water as compared with a 0% load. The purpose of this study is to examine the effect of an extended range of phenobarbital doses upon drinking after different degrees of water deprivation.

METHOD

The animals for this experiment were 16 male albino rats obtained from Maxfield Animal Supply, Cincinnati, OH. The rats were 90 days of age at the beginning of the experiment. The rats were divided so that two rats lived in a home cage. Both rats in each home cage were maintained under the same deprivation conditions.

The apparatus consisted of 16 drinking boxes 10 cm × 10 cm × 30 cm. The floor and roof were made of hardware cloth, the walls were made of unpainted wood. A drinking spout, connected to a 50 ml gas measuring tube, extended into the box about 2.5 cm above the floor. A masonite door, approximately 4 cm from the wall, separated the drinking spout from the rest of the compartment.

The rats were placed upon suitable water deprivation schedules. One group of 8 animals received a single half hour drinking period per day after 23½ hr water deprivation. The other group of 8 rats obtained water twice a day in half hour drinking periods separated by 11½ hr without water. At one drinking period all rats were removed from their home cages, weighed, placed in drinking boxes, and allowed to drink for the requisite time. During the other drinking period, the drinking period for the 11½ hr deprived rats only, a water bottle placed on the home cage served to maintain deprivation conditions. These schedules were maintained without further treatment for 15 days and continued throughout the course of the experiment.

On the sixteenth day of the deprivation and every third day thereafter, the experimental treatments were administered. The treatments corresponded to a predetermined 8 × 8 Latin Square sequence in which each rat received each phenobarbital dosage once and each treatment was administered equally often upon each treatment day. The phenobarbital doses varied from 0 to 70 mg/kg in 10 mg/kg steps. The 0 mg/kg solution was 0.9% saline solution, the solvent for the phenobarbital sodium. Solutions were adjusted in concentration so that 1 ml/kg was administered upon each injection day. Subcutaneous injection was the route of administration of the drug. The animals received their injections 45 min prior to the time at which they were allowed to drink.

RESULTS

The results of the experiment are summarized in Fig. 1. It is clear that both curves initially rise with increasing phenobarbital dosage and fall with still further increases. The dose effect is large and significant, $F(7,81) = 8.44$,

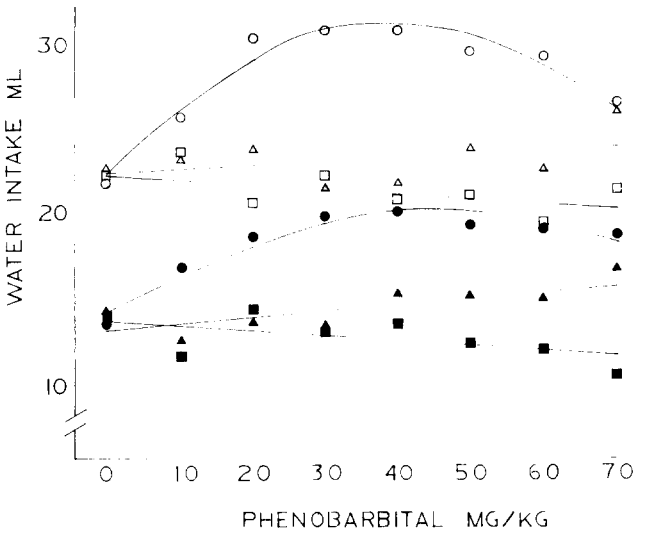

FIG. 1. Mean water intake as a function of hours of water deprivation and phenobarbital dosage. Circles symbolize water ingestion 45 min after injection, triangles symbolize water ingestion a day later, and squares symbolize water ingestion 2 days later. The open figures represent the findings for 23½ hr water deprivation while the filled figures represent water intake for 11½ hr water deprivation. The lines are the lines of best fit.

$p<0.001$. The best fitting quadratic equation of the form $Y = A+BX-CX^2$ accounts for 92% of the dosage variance. Deprivation as expected gives a highly significant results, $F(1,14) = 21.97$, $p<0.001$. The 11½ hr water deprived rats drink less than 23½ hr water deprived rats which is scarcely surprising. The interaction of dosage with hours of deprivation, $F(7,81) = 1.00$, n.s., is negligible. This would suggest that the phenobarbital dose-drinking response curves are simply displaced as a function of hours of deprivation and only the intercept varies.

On the day following the day of injection both groups of animals show a significant linear increase of water intake as a function of phenobarbital dosage, $F(1,91) = 9.60$, $p<0.01$. The interaction between the two curves is negligible, $F(1,91) = 1.00$, $p>0.20$, indicative of similar functions differing only in their origin. Two days after injection, water ingestion declines as a linear function of phenobarbital dose, $F(1,89) = 9.45$, $p<0.01$. Again the interaction of hours of deprivation with the effect of phenobarbital dose is negligible, $F(1,89) = 1.00$, $p>0.20$). Increased hours of deprivation have the expected dipsogenic effect, $F(1,14) = 14.74$, $p<0.001$).

DISCUSSION

Quadratic dose response functions were found for the phenobarbital effect upon drinking at 11½ and 23½ hr of water deprivation on the treatment day. The curves differ from each other negligibly except in terms of the varied effect of magnitude of water deprivation, in short the curves appear to differ by a constant displacement. On the second day of the 3 day cycle, the phenobarbital dose-drinking response curves increase as a linear function of the dose in both 11½ and 23½ hr water deprivation. Again the interaction between the curves is negligible. Finally, two days after injection, both dose-response curves fall as a linear function of the dose being displaced by a constant determined by the difference in water deprivation.

These results are simply consistent with the notion that phenobarbital or barbiturates in general serve to stimulate drinking [2]. In the simplest terms, this theory proposes that the response is simply proportional to phenobarbital dosage. In contrast the proposition that phenobarbital or barbiturates in general facilitate drinking by disinhibiting drinking is qualified to some extent. If one proposes that increasing drinking as a function of hours of deprivation is due to diminishing inhibition of the drinking response, an extension of the thinking of Anand and Dua [1] from eating to drinking, the disinhibiting effects of phenobarbital, if such they be, may be not upon inhibiting effects pertaining to regulation itself. One bit of evidence against such reasoning is the finding that phenobarbital reduces the drinking latency of rats treated with hypertonic saline [4]. The decisiveness of that evidence is contingent upon the communality of mechanisms underlying saline and deprivation induced drinking. Another theoretical approach implicating phenobarbital as a disinhibitor of drinking but based upon variations in excitation as the source of drinking variations as a function of hours of deprivation [3] would require that net inhibition of drinking is essentially constant between 11½ and 23½ hr of water deprivation. What would be further required is that after some short period of inhibition of drinking by water in the stomach or by oroesophageal cues, or both, there be some period of quiescence terminated by a suprathreshold level of dysregulation giving rise to drinking.

On the day following injection the changes in drinking response as a function of phenobarbital dosage is similar both for 11½ and 23½ hr of deprivation. On the day following injection, drinking in this experiment increased as a function of phenobarbital dosage. This is somewhat in contrast to the findings of Schmidt and Dry who find some rise in drinking at the higher phenobarbital doses as did this experiment but some decline at low to moderate doses [5] when drinking was analyzed 24 hr 45 min after injection. The declining level of drinking as a function of phenobarbital dose for 2 days after injection is similar to that described previously [5]. These data would suggest that recovery from phenobarbital follows a similar time course independent of water deprivation and water metabolism over some extended range of deprivation.

REFERENCES

1. Anand, B. K. and S. Dua. Feeding responses induced by electrical stimulation of the hypothalamus in the cat. *Indian J. med. Res.* **43:** 113–122, 1955.
2. O'Kelly, L. I. and H. H. Weiss. The effects of ether and a barbiturate on water regulation in the rat. *J. comp. physiol. Psychol.* **48:** 123–125, 1955.
3. Schmidt, H. Jr. Variations in water ingestion: The response to barbituates. W. A. Hinwich and J. P. Schade (eds.). Horizons in Neuropsychopharmacology. *Prog. Brain Res.* **16:** 263–284, 1965.
4. Schmidt, H. Jr. Barbiturate effects on saline acceptance and post ingestion variables. *Physiol. Behav.* **1:** 183–189, 1966.
5. Schmidt, H. Jr. and L. Dry. Dose and time as variables in barbiturate action upon water ingestion. *Am. J. Physiol.* **204:** 817–820, 1963.
6. Schmidt, H. Jr. and S. J. Moak. Some drug effects influencing barbiturate facilitation of water ingestion. *Am. J. Physiol.* **196:** 307–310, 1959.