

Pharmacology Laboratory,  
School of Medicine—U.F.R.J.  
Av. Pasteur, 458  
Rio de Janeiro, Brazil  
February 9, 1968

J. R. BUENO\*  
N. J. NOGUEIRA DE CASTRO\*  
L. SOLLERO

\* Fellows of the Conselho Nacional de Pesquisas.

### References

- Augstein, J. & Green, J. M. (1964). *Nature, Lond.*, **201**, 628–630.  
Bueno, J. R., de Castro, N. J. N. & Sollero, L. (1967). *Hospital*, **72**, 175–184.  
Frohlich, E. D., Dustan, H. P. & Page, I. H. (1966). *Clin. Pharmac. Ther.*, **7**, 599–607.  
Peart, W. S. & MacMahon, M. T. (1964). *Br. med. J.*, **1**, 398–402.

### The effect of the chronic administration of sodium barbitone on the exploratory behaviour of rats

SIR,—Contrary to previous experience with rats (Leonard, 1967) it now appears that the chronic administration of sodium barbitone affects the reward-motivated rather than fear-motivated behaviour, and therefore it was of interest to investigate the action of the barbiturate on unlearned behaviour, for example, exploratory activity. The Y-box test of Steinberg, Rushton & Tinson (1961) appeared to provide a simple, quantifiable method for the determination of exploratory activity.

Female rats (initially 45–55 g) originally of the Wistar strain were housed singly throughout the experiment. Sodium barbitone was added to the drinking water in increasing concentrations over a period of 5 weeks and then withdrawn. The initial dose of barbitone was 100 mg/kg/day and this was increased by increments of 100 mg/kg/day every week. Sodium saccharin (20 mg/100 ml) was added to the drinking water to disguise the bitter taste of the barbiturate and also to the drinking water of the untreated animals. To ensure maximal activity all animals were kept on reversed (12 hr) lighting. The experimental and untreated rats were individually put into the Y-box during the period of barbiturate administration and after its withdrawal as shown in Fig. 1. The total number of entries into the arms of the Y-box in 3 min was recorded. The exploratory activity was measured on the second day after withdrawal of the barbiturate from the experimental rats, as it has been shown previously that this coincided with the period of maximal withdrawal hyperexcitability (Leonard, 1967). All rats were allowed free access to food and water apart from the time during which they were in the Y-box. They were disturbed as little as possible and the experiment was conducted in the room in which they were housed. A diffuse red light enabled the animals to be observed during the time in which they were in the Y-box.

The results (Fig. 1) show that sodium barbitone does not affect the exploratory behaviour and that familiarity with the Y-box does not lead to a noticeable reduction in exploratory activity since the mean response of the untreated animals did not change appreciably during the course of the experiment. When the barbiturate was withdrawn the mean number of entries was reduced by about 70% and was still significantly reduced 4 weeks later. This post-withdrawal depressant effect is surprising because apart from the hyperexcitability and occasional spontaneous convulsions that occurred during the first few

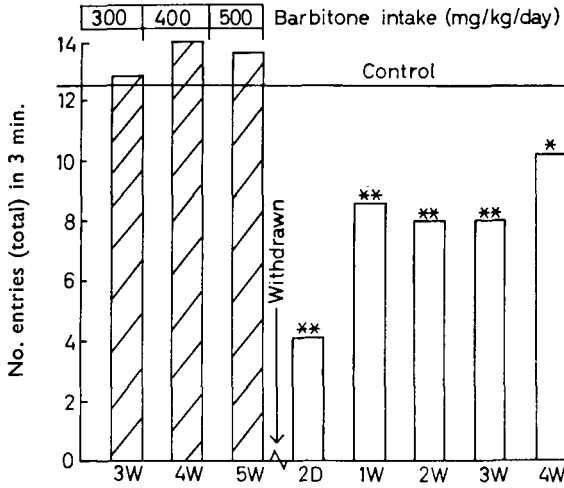


FIG. 1. Effect of the long term administration of sodium barbitone on exploratory behaviour. The ordinate shows the mean number of entries into the arms of the Y-box and the abscissa shows the time, in weeks (W) or days (D), at which the exploratory behaviour was determined. The results are given as the mean values for 6 experimental and 6 untreated rats. The significance of the results, using Student's *t*-test, shown as \*\* $P < 0.001$  and \* $P < 0.05 > 0.02$ . Hatched columns before and open columns after sodium barbitone had been withdrawn from the drinking water.

days after withdrawal, there appeared to be no superficial difference in behaviour between the treated and untreated groups of rats for example, when handled, or in response to an auditory stimulus such as a click. Furthermore, no difference was observed between the experimental and untreated groups of rats in the excitability of the central nervous system as assessed by electroshock or chemical convulsants, 10 days after withdrawal (Leonard, 1968).

These results suggest that the effect of a barbiturate on exploratory behaviour after chronic administration is different from the acute effects. Rushton & Steinberg (1963) found that amylobarbitone increased the exploratory behaviour in low doses but that doses greater than 30 mg/kg produced a depression of the exploratory behaviour.

Pharmacy Department,  
University of Nottingham,  
University Park,  
Nottingham, England.  
February 7, 1968

B. E. LEONARD

**References**

Leonard, B. E. (1967). *Int. J. Neuropharm.*, 6, 63-70.  
 Leonard, B. E. (1968). *Ibid.*, in the press.  
 Steinberg, H., Rushton, R. & Tinson, C. (1961). *Nature, Lond.*, 192, 533-535.  
 Rushton, R. & Steinberg, H. (1963). *Ibid.*, 197, 1017-1018.