two vertical panels (5 cm × 5 cm) mounted on wall of the testing box. The initial stimulus of each trial was presented at 20 s intervals on the right hand panel. It was either a cross or a square of 2 s duration and these stimuli were presented in random order. After the initial right hand stimulus there was a delay before the left hand panel was illuminated. The left hand stimulus was also a square or a cross of 2 s duration. The delay between the stimuli was fixed for each session at either 2, 4 or 8 s. The cross and square sequence of each panel and the like or unlike sequence of each trial were both in random order. Each sequence of trials consisted of 25 squares and 25 crosses on each panel. A total of 50 trials was presented in each session and in the event of an error the trial was repeated until a correct response was made.

If the stimuli were like (cross followed by a cross or square followed by a square) the animal was required to depress the lever during the 2 s presentation of the left hand stimulus. If the stimuli were unlike (cross followed by a square or square followed by a cross) the animal was required to refrain from pressing the lever. A correct response (go response if like stimuli or no-go response if unlike stimuli) was rewarded by a pellet.

The effect of three barbiturates, heptabarbitone (20 and 30 mg/kg), pentobarbitone sodium (10 and 15 mg/kg) and quinalbarbitone sodium (10 and 15 mg/kg) were studied in five male rhesus monkeys (*Macaca mulatta*) and were administered by intraperitoneal injection. No differential effects could be shown between the three drugs, nor could the effect of the drugs be related to the delay between stimuli. Both doses of each drug produced highly significant increases in total response time 2 h after administration, but only the higher dose of each barbiturate had an effect at the 6 h interval. Changes in accuracy of matching were not observed after the lower dose of each drug, but at the higher doses there was a reduction in accuracy of matching significant at the 5% level.

We have found no evidence that pentobarbitone sodium has a specific effect on short term memory, but the possibility does exist that such an effect could be uncovered by using animals which have not been over-trained and on a task which involves a go/no-go response. The duration of the initial stimulus and the proximity of the testing period to the injection of the drug may also be factors in the possible appearance of behavioural deficits related to the delay between stimuli.

REFERENCES

GLICK, S. D., GOLDFARB, T. L., ROBUSTELLI, F., GELLER, A. & JARVIK, M. E. (1969). Impairment of delayed matching in monkeys by chlorpromazine and pentobarbital. *Psychopharmacologia. (Berl.)*, **15**, 125–133.

ROBERTS, M. H. T. & BRADLEY, P. B. (1967). Studies on the effects of drugs on performance of a delayed discrimination. *Physiol. Behav.*, **2**, 389–397.

The influence of propranolol on abnormal behaviour induced in rats by prolonged isolation—an animal model for mania?

ZIPORA SPEIZER and MARTA WEINSTOCK*

Department of Physiology and Pharmacology, Sackler School of Medicine, Tel-Aviv University, Beilinson Hospital, Petach-Tikvah, Israel

The clinical efficacy of a number of β-adrenoceptor blocking agents has recently been reported in the management of acute manic and schizophrenic patients (Atsmon, Blum, Wijsenbeek, Maoz, Steiner & Ziegelman, 1971; Degwitz, 1971; Auriol, Paladjian, Bord & Vals, 1972). It has been suggested that mania may result from either an excessive release of central amine transmitter or from receptor supersensitivity, or both (M.R.C. Brain Metabolism Unit, 1972). The beneficial effects of these agents could therefore result either by blocking the amine receptors or by preventing such an excessive release of transmitter.

To obtain further information about the action of β-receptor blocking agents, we studied the effect of (±)-propranolol, in an animal model in which abnormal behaviour was produced by prolonged isolation. This model was chosen because it has been suggested that such treatment also results in receptor hypersensitivity, which alone, or together with excessive transmitter release, may be the cause of the hyperactivity (Welsh & Welsh, 1965).

Isolation of male rats for 6–8 weeks after weaning, resulted in a marked increase in exploratory motor activity, rearing, sniffing and ambulation, when placed in an open field (novel) situation, compared to group-housed controls. Isolated rats were also more sensitive to the effects of isoprenaline, but not noradrenaline on the cardiovascular system.

(±)-Propranolol, 0·2–0·5 mg/kg (s.c. given 15 min before exposure to open field) reduced the hyperactivity of these rats to the control level found in group housed animals. Higher doses did not further reduce activity. Propranolol had no influence on motor activity of normal rats in doses below 20 mg/kg. The reduction of the hypermotility by (±)-propranolol could be attributed to any one of its pharmacological actions; blockade of β-adrenoceptors, membrane stabilization or a reduction in catecholamine release. We therefore compared its effects with those of (+)-propranolol which has only weak β-receptor blocking activity, and with practolol, which lacks the local anaesthetic effect, while both drugs retain the ability to reduce catecholamine release (Eliash & Weinstock, 1971 ; Weinstock, 1973).

Both (+)-propranolol and practolol, 0·5–1 mg/kg, reduced the hyperactivity of isolated rats without affecting motor activity of normal controls. This finding suggested that all three drugs may affect this form of abnormal behaviour by reducing an excessive release of central catecholamine.

REFERENCES

ATSMON, A., BLUM, I., WIJSENBEEK, H., MAOZ, B., STEINER, M. & ZIEGELMAN, G. (1970). The short term effects of adrenergic blocking agents in a small group of psychotic patients. *Psychiatr. Neurol. Neurochir.*, **74**, 251–258.

AURIOL, B., PALANDJIAN, N., BORD, M. & VALS, A. (1972). Les Beta bloquants en psychiatrie. *La Nouvelle Presse Medicale*, **21**, 1439.

DEGWITZ, R. (1971). Experience with high doses of a beta-receptor blocking agent (Trasicor) in cases of excited psychosis. *Vth World Congress of Psychiatry La Prensa Medica Mexicana*, **229**.

ELIASH, S. & WEINSTOCK, M. (1971). Role of adrenergic neurone blockade in hypotensive action of propranolol. *Br. J. Pharmac.*, **43**, 287–294.

M.R.C. BRAIN METABOLISM UNIT (1972). Modified amine hypothesis for the aetiology of affective illness. *The Lancet. II*, **16**, 573–577.

WEINSTOCK, M. (1973). A comparison of the adrenergic neurone blocking actions of propranolol and practolol. *Br. J. Pharmac.*, in the press.

WELSH, B. L. & WELSH, A. S. (1965). Effect of grouping on the level of brain norepinephrine in white Swiss mice. *Life Sci.*, **4**, 1011–1018.

Atropine sensitivity of transmission and facilitation in the rabbit superior cervical ganglion

M. J. BRIMBLE* and D. I. WALLIS

Department of Physiology, University College, Cardiff

Evidence has accumulated in recent years suggesting that muscarinic receptors play a part in transmission through sympathetic ganglia and particularly in the facilitation following trains of conditioning stimuli (Libet, 1964). The Late Negative (LN) wave seen after single or trains of ganglionic action potentials is thought to be involved in this facilitation, as both coincide in time of onset and the LN wave is very sensitive to atropine.

We investigated this problem using the excised ganglion maintained at 37° C in a bath which allowed continuous superfusion with Krebs solution. Stimuli supramaximal for the main (Sa) component of the postganglionic compound action potential were delivered to the preganglionic trunk 30 mm proximal to the ganglion; responses were recorded either from the ganglion or from the internal carotid nerve 3 mm distal to the ganglion. The action potentials recorded remained relatively stable for several hours, although a slow decline in amplitude was sometimes seen. Perfusion with 0·29 μM atropine sulphate, (0·1 μg/ml), caused a reduction in Sa amplitude. This reduction was maximal after approximately 25 min. 2·9 μM atropine (1 μg/ml) caused no further reduction. Allowing for any steady decline, spike amplitude was decreased by 9±1% (mean, S.E. of mean, n=14) by 2·9 μM atropine.

The pattern of facilitation following a single conditioning stimulus reveals phases of