inhibitors were used to release ACh. This fact indicated that the activity of membrane ATP-ase might have a role in the release mechanism. It was suggested that, under physiological conditions, calcium might act by inhibiting the membrane ATP-ase and thereby promoting release of ACh.

Recent work on ACh release from eserinized (2 μg/ml) longitudinal muscle strips of guinea-pig ileum suggests that conditions which stimulate membrane ATP-ase reduce the volley output of ACh.

When 5·9 mM potassium was added to tissues which had been suspended in potassium-free Krebs' solution for 1 h the output/volley of ACh at 0·1 Hz stimulation was reduced from $49{\cdot}5 \pm 3{\cdot}8$ to $3{\cdot}1 \pm 0{\cdot}5$ (pmol/g)/volley ($n=3$; $p<0{\cdot}01$). However, the output during stimulation at 10 Hz for 1 min was only slightly reduced; outputs being $7{\cdot}5 \pm 0{\cdot}4$ and $5{\cdot}9 \pm 0{\cdot}6$ (pmol/g)/volley, respectively. The impairment of ACh output in response to stimulation at 0·1 Hz on adding of 5·9 mM potassium lasted not more than 10–15 min and the output recovered slowly. The resting output during the control period, (252 (pmol/g)/min) was enhanced when potassium was withdrawn (403·5 (pmol/g)/min) and reduced on adding 5·9 mM potassium (82·5 (pmol/g)/min). This is a result which was not expected on the basis of the Nerst equation for a potassium electrode.

Both magnesium-excess (9·3 mM) and noradrenaline (10^{-6} M) influenced the output of ACh: a reduction was observed at low (0·1 Hz), but not at high (10 Hz) frequencies of sustained stimulation.

Since potassium, excess magnesium and noradrenaline, all stimulated (Na^+-K^+-Mg^{2+})-activated ATP-ase and were capable of reducing output of acetylcholine it is suggested that the actual activity of membrane ATP-ase may control the release of ACh. It is not unreasonable to assume that the higher the activity of membrane ATP-ase and the more stabilized the membrane, the less the ACh is released. This might also explain why the output/volley is low when high frequency stimulation is applied as this is also known to stimulate membrane ATP-ase (Ritchie & Straub, 1957).

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Impaired performance of delayed matching in monkeys by heptabarbitone, pentobarbitone sodium and quinalbarbitone sodium

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The ability of monkeys to match stimuli separated by short intervals of time has been used by several workers to study the effect of drugs. Roberts & Bradley (1967) found that chlorpromazine and pentobarbitone sodium impaired performance on a delayed matching task and they suggested that, though chlorpromazine acted as a sedative, pentobarbitone sodium may have had a specific effect on recent memory. In view of the sedative properties of both drugs and their depressive effect on motor responsiveness, Glick, Goldfarb, Robustelli, Geller and Jarvik (1969) carried out further studies using a delayed matching to sample task which involved responses over a 16 h period after administration of the drug. They agreed with the findings of Roberts & Bradley (1967) on chlorpromazine, but were unable to support the suggestion that pentobarbitone sodium specifically impaired short term memory.

We have re-examined this because of the importance of the possible neurological effects of hypnotics used by persons engaged in skilled activity. A delayed matching task similar to that described by Roberts & Bradley (1967) was used. The stimuli were white illuminated patterns (cross or square) on dark backgrounds and were displayed on

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.

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

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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).