Short Communications

Potentiation by Lithium of the Haloperidol-Induced Behavioural Suppression

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With 2 Figures

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Lithium salts have been used for many years in the treatment of mania and in the prophylaxis of mania and depressive states (for rev. see Schou, 1968). It is not known how lithium exerts its effects but several studies suggest that lithium, like many other psychoactive drugs, may act by interfering with central monoamine neurotransmission (for rev. see e.g. Davis and Fann, 1971). It is generally assumed that neuroleptic drugs, like phenothiazines and butyrophenones, owe their antipsychotic action to a blockade of central catecholamine receptors (see Carlsson, 1973). This in turn activates a compensatory mechanism resulting in an increased synthesis and release of the transmitter (Carlsson and Lindquist, 1963; Carlsson, 1973). When the compensatory mechanism is inhibited by e.g. inhibition of tyrosine hydroxylase, the behavioural action in animals (Ahlenius and Engel, 1971, 1973) and antipsychotic effects in man (Carlsson et al., 1972, 1973) are markedly potentiated.

In the present experiment we have investigated a possible interaction between lithium and haloperidol on operant behaviour in rats in order to evaluate the effects of lithium on central catecholamine mechanisms.

Three male Sprague-Dawley rats, 280—290 g, were kept at 80 % of their free feeding weight and trained to press a lever to obtain food in standard behavioural chambers (Grason-Stadler, Mass., U.S.A). The animals after initial training were maintained on a fixed
ratio 40 schedule (FR 40), i.e. every 40th lever press will produce a food-pellet (Noyes, 45 mg). This schedule generates a high and stable rate of responding (Ferster and Skinner, 1957). Responses and reinforcements were recorded on digital counters and cumulative recorders. The rats were exposed to daily sessions of 30 min, 5 days a week. Drug administration was not begun until a stable behavioural baseline was established for each animal. The 10 pre- and 10 post-experimental sessions served as control sessions.

Haloperidol (Janssen, Beerse) was given intraperitoneally 15 min before the behavioural test. The drug was dissolved in a few drops of acetic acid and the final solution made up with 5.5 % glucose. Li₂CO₃ was injected intraperitoneally 4 h before the behavioural test and was dissolved in 0.9 % saline and 6 N HCl was added until the pH had reached 7. The doses are given in the figures.

In a separate experiment the highest ineffective doses of haloperidol and Li₂CO₃ were found to be 0.04 mg/kg and 150 mg/kg, respectively. These doses were then chosen in the design of the main experiment.

As found in the pilot experiment the intraperitoneal injection of haloperidol (0.04 mg/kg) had no significant effect on the lever-

![Graph](image-url)

Fig. 1. Effects of Li₂CO₃ and haloperidol, alone or in combination, on food-reinforced lever-pressing behaviour (Fixed Ratio 40 : 1) in rats. Li₂CO₃ was injected i.p. 4 h before and haloperidol i.p. 15 min before the start of the session. Shown are the means ± s.e.m. of three rats. Statistical analysis was performed by t-test after analysis of variance:

- A—D, B—D, C—D (p < 0.01);
- A—B, A—C, B—C N.S. (p > 0.05)