by 5-hydroxytryptophan (5-HTP). However, results with 5-HTP are not clearly interpretable as, unlike tryptophan, it can be decarboxylated to 5-HT in neurones other than those containing 5-HT (Fuxe, Butcher & Engel, 1971). The present finding that tryptophan reverses the effect of PCPA is stronger evidence that 5-HT neurones are involved. Furthermore, the results demonstrate an alteration of behaviour by tryptophan only in 5-HT deficient animals and therefore may be relevant to the effect of tryptophan in depression.

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The effects of lithium, rubidium and caesium on the response of rats to tranylcypromine and α-methyl-*p*-tyrosine given separately or in combination

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Administration of 20 mg/kg tranylcypromine (Tc) to rats primed for three days with lithium chloride (LiCl) injections produces hyperactivity which is inhibited by para-chlorophenylalanine (Grahame-Smith & Green, 1974b). A similar syndrome is produced by combining L-tryptophan and Tc. This latter response is inhibited by α-methyl-*p*-tyrosine (αmpt) (Grahame-Smith & Green, 1974a). The effect of Tc on LiCl, rubidium chloride (RbCl) or caesium chloride (CsCl) loaded rats is reported here. Rats given LiCl, RbCl or CsCl in their diet (30 mmol/kg dry food) for 14 days and then injected s.c. with 15 mg/kg Tc exhibited marked hyperactivity. All facets of activity do not increase but there is a characteristic continuous locomotion with the body close to the cage floor.

The hyperactivity is greater and of more rapid onset following RbCl than LiCl. This difference was associated with different rates of accumulation of 5-hydroxytryptamine (5-HT), the increases above control values were 46% (Li) and 85% (Rb).

Hyperactivity was inhibited by αmpt (250 mg/kg i.p. 36 h before, plus 150 mg/kg 2 h before, Tc) more effectively following LiCl than RbCl. This combination of αmpt and Tc produced rat brain concentrations of dopamine (DA) significantly below control values in sodium chloride (NaCl) and LiCl pretreated rats but not following RbCl. This suggests that a system which is both 5-HT and DA sensitive is responsible for the hyperactivity.

The increase in brain noradrenaline (NA) concentration following Tc injection was significantly less following RbCl than after NaCl or LiCl. A smaller proportion of NA metabolized by the monoamine oxidase pathway following RbCl treatment could produce this effect. αmpt causes a decrease in rat brain NA concentration which is greater following LiCl or RbCl treatment than after NaCl. This could be due to lithium or rubidium increasing NA 'turnover' rates. All results reported are significant at levels beyond $P = 0.05$.

Previous studies have emphasized the opposite effects of lithium and rubidium on animal activity and brain monoamines. This study shows similar effects on activity when Tc is administered, and both ions increased 5-HT accumulation and NA turnover rates.

The fact that lithium is effective in the treatment of bipolar affective illnesses does perhaps indicate that it has more than one action. Drug-induced hyperactivity in animals has frequently been seen as an analogue to mania, and lithium has often been found to be effective in

attenuating those hyperactivity syndromes. The interaction between lithium and Tc is the first to show an activating effect of lithium in animals and might be viewed as a possible experimental model of antidepressant activity. We believe that it is important at this stage to merely show that lithium will produce changes in animal activity and metabolism which could conceivably be analogous to alteration of mood in man. The fact, however, that both caesium and rubidium ions have the same effects suggests that the responses studied are not very specific to lithium. They do, however, also suggest reasons for further clinical studies of rubidium and caesium.

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Effects of lysergic acid diethylamide on auditory and visual discrimination in the rat

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The effect of LSD on either visual or auditory discrimination was studied in rats matched for discrimination performance. A drug may affect discrimination either by changing stimulus sensitivity or by shifting the criterion for responding. A method of analysis, derived from signal detection theory (SDT), was used to assess independent effects on these two factors.

Twelve adult, male, hooded rats (300 g) were used. Each animal was first trained on a DRL (differential reinforcement of low rate) schedule. A signal indicated the availability of reinforcement. After each reinforced response, the interval to the next signal was varied unpredictably between 9 and 27 s (mean delay 18 s). A response, 9 s or less before the signal, postponed reinforcement for a further 9 s. The schedule yielded a low but constant response-rate. One group of rats (n = 6) was trained with a light signal, the second group (n = 6) with a tone, and the two groups were matched for discrimination performance. Each rat was trained 45 min per day for 44 days before the experiments, to produce consistent baseline responding. A SDT analysis, described fully elsewhere (Warburton & Brown, 1972), was used to determine two parameters, A', a measure of stimulus sensitivity, and B'', a measure of response bias. The drugs were lysergic acid diethylamide tartrate (Sandoz) and methysergide bimaleate (Sandoz) (a control for peripheral effects). The injection conditions were 0.005, 0.01, 0.05, 0.25 mg/kg LSD, 0.50, 1.00 mg/kg methysergide, and distilled water. The solutions were made up in distilled water and injected i.p. in the volume 1.0 ml/kg. Each rat was tested under each injection condition, with order of injection counterbalanced within each group. Injections were given at 48 h intervals. For statistical analysis results on an injection day were compared with the preceding day's baseline performance.

LSD effects were found to be comparable for the two groups. Total responses were reduced by on average 62.7% ($P < 0.001$) at the highest dose of LSD (0.25 mg/kg). There were no other significant drug effects on response rate. There was a reduction in A' (i.e. a decrease in stimulus sensitivity) at 0.25 ($P < 0.005$) and at 0.05 mg/kg LSD ($P < 0.005$). No other changes in A' under any other injection conditions occurred. The sensitivity changes were not due to changes in response bias (B''), since there were no consistent drug effects on it.

The study demonstrated a reduction in the number of responses at the highest dose of LSD, and independently of this, a decrease in sensitivity to either a tone or a light signal at 0.05 and 0.25 mg/kg LSD. There were no drug effects upon response bias.

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