tical conditions.

The behavioural characteristics of the kainic acid injected animals were tonic extensions of the hind limbs which were pronounced 24 h after injection but tended to dissipate at longer survival times. At all survival times, a general lack of muscle tone and coordination was apparent – these symptoms being consistent with a cerebellar lesion. In no instance with the dihydrokainic acid injected rats, was any behavioural abnormality evident.

The neuronal cell types lesioned under these conditions are all inhibitory and, may utilize γ-aminobutyric acid (GABA) as a transmitter. Accordingly, we have examined the high affinity uptake of [^{3}H]-GABA into cerebellar synaptosomes and, have found that the V_{max} in kainate-lesioned cerebellum was reduced to 55% of control and dihydrokainate injected rats, whilst the K_m remained unaltered (Table I). This finding correlated well with the histological data which showed that approximately 50% of the cerebellum was affected by the lesion. In close correspondence with the preservation of the granule cells, was the finding that the high affinity uptake of [^{3}H]-glutamate was unaffected by the kainic acid lesion (Table I). These findings provide further evidence for the hypothesis that glutamate is the transmitter of the cerebellar granule cells.

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Table 1 Effect of kainic acid lesion on the uptake of [^{3}H]-GABA and [^{3}H]-glutamate into rat cerebellum

[^{3}H]-GABA	*K_m (μM)*	*V_{max} (nmole mg protein^{-1} 5 min^{-1})*
Control	2.35 ± 1.05	13.04 ± 1.80
kainic acid	2.63 ± 0.99	5.50 ± 0.67*
dihydrokainic acid	2.39 ± 0.47	12.20 ± 0.75
[^{3}H]-gluatamate	*K_m (μM)*	*V_{max} (nmole mg protein^{-1} 3 min^{-1})*
Control	11.84 ± 4.88	14.52 ± 2.11
kainic acid	8.68 ± 1.11	12.41 ± 0.52
dihydrokainic acid	6.90 ± 1.10	16.35 ± 0.69

Significance of difference from control by *t*-test; *$P<0.01$

Some observations on the behavioural and biochemical effects of L-tryptophan plus a monoamine oxidase inhibitor in immature rats

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Adult rats given L-tryptophan (L-TP) plus a monoamine oxidase inhibitor (MAOI) develop a characteristic behavioural syndrome including hyperactivity which results from increased brain 5-hydroxytryptamine (5-HT) synthesis and function (Grahame-Smith, 1971). This behavioural model has been used to study the mechanisms controlling central 5-HT function and the effects of drugs on this function (Green & Grahame-Smith, 1976). We have now investigated the behavioural and biochemical responses of immature rats to L-tryptophan plus a MAOI with a view to studying the effects of drugs on developing brain 5-hydroxytryptaminergic systems.

Adult male Sprague-Dawley rats (150–200 g) or 21-day old male pups (40–50 g) were injected with tranylcypromine (TCP 10 mg/kg i.p.). Thirty minutes later L-TP was administered (5–100 mg/kg i.p.) and activity recorded (movements/min) using LKB Animex activity meters (sensitivity and tuning: 30 μA). At 120 min brains were removed and tryptophan (Denckla & Dewey, 1967) and 5-HT (Curzon & Green, 1970) measured.

Basal brain 5-HT concentrations were 0.37 ± 0.02 μg/g wet weight (21 day; $n = 6$) and 0.43 ± 0.01 μg/g (adult; $n = 8$; $P < 0.05$). Tryptophan concentrations were 4.45 ± 0.4 (21-day; $n = 6$) and 2.86 ± 0.03 (adult; $n = 8$; $P < 0.01$).

Brain tryptophan concentration 90 min after L-TP injection was directly related to the L-TP dose in both adults and pups. However, accumulation of brain tryptophan over this 90 min period (corrected for basal levels) revealed that 21-day rat brain accumulated more tryptophan than adult brain at corresponding doses of L-TP (126% of adult brain tryptophan accumulation at 25 mg/kg and 188% at 50 mg/kg L-TP).

The accumulation of adult brain 5-HT over 90 min increased up to an L-TP dose of 100 mg/kg whereas 21-day brain 5-HT accumulation plateaued at around

20 mg/kg L-TP. The two age groups also reached their maximum 5-HT accumulation at different brain tryptophan concentrations.

Both adult and immature rats exhibited similar behavioural changes following L-TP injection. Activity increased at both ages with increasing L-TP dose up to around 70 mg/kg. This increased activity without an increase in brain 5-HT in immature rats might be due to increased sensitivity postsynaptic to the 5-HT neurones. However, behavioural responses to putative 5-HT agonists (5-methoxy-N, N-dimethyl tryptamine and quipazine) did not reveal any difference between adults and pups.

In 21-day rats pretreated with a peripheral decarboxylase inhibitor (50 mg/kg benzerazide Ro4-4602 15 min before TCP) activity counts at both 35 and 70 mg/kg L-TP were reduced by approximately 50%. This indicates a possible involvement of tryptamine in the immature rat behavioural responses to L-TP as previously suggested for the adult rat (Marsden & Curzon, 1978).

These results, therefore, show that immature rats respond behaviourally in a similar way to adults following L-TP and TCP administration, but that the biochemical correlates of such treatment are different.

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Backward walking and circling: a behavioural response to concurrent catecholamine and 5-hydroxytryptamine release

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Amphetamine, fenfluramine and p-chloroamphetamine at high dosages cause backward walking and circling in rats (Taylor, Goudie, Mortimore & Wheeler, 1974; Growdon, 1977). Bizarre behaviour of this kind is of particular interest as a possible animal model for amphetamine psychosis. It also occurs when animals are given many other drugs with hallucinogenic properties (Schneider, 1968; Smythies, Johnstone, Bradley, Benington, Morin & Clark, 1967). In this study we have obtained evidence for the roles of dopamine (DA) and 5-hydroxytryptamine (5-HT) in the mediation of backward walking and circling.

Male Sprague-Dawley rats (180–200 g) were housed three to a cage and behaviour scored for 1 h after i.p. injection of drugs using the method of Taylor *et al.* (1974) modified to include 5-HT dependent behaviours described by Trulson & Jacobs (1976). (+)-Amphetamine (15 mg/kg) caused backward walking and circling which were significantly increased by L-tryptophan (50 mg/kg) and decreased by the inhibitor of 5-HT synthesis p-chlorophenylalanine (200 mg/kg), by the 5-HT receptor blockers methergoline (1 mg/kg) by the 5-HT receptor blockers metergoline (1 mg/kg) and cyproheptadine (10 mg/kg), by fluoxetine (10 mg/kg) (which selectively inhibits uptake of drugs into 5-HT neurones) and by the dopamine receptor blockers α-flupenthixol (0.2 mg/kg) and pimozide (25 mg/kg).

Amphetamine (5 mg/kg), fenfluramine (5 mg/kg, 10 mg/kg) and p-chloroamphetamine (5 mg/kg, 10 mg/kg) when given alone did not cause backward walking and circling but these behaviours did occur when amphetamine (5 mg/kg) was given together with either fenfluramine (5 mg/kg) or p-chloroamphetamine (5 mg/kg). The two latter drugs also caused various behavioural changes characteristic of 5-HT release (Trulson & Jacobs, 1976) which were unaffected by amphetamine (5 mg/kg). This suggests that (unlike backward walking or circling) these behaviours are not enhanced when the activation of catecholamine receptors is increased above physiological levels. Fenfluramine and p-chloroamphetamine markedly decreased rearing, gnawing and licking induced by amphetamine.

There is evidence that many drugs which cause hallucinations in man and backward walking and circling in laboratory animals also (either directly or indirectly) activate both DA and 5-HT post-synaptic receptors. The present results suggest the possibility that these effects are together responsible for the above behavioural changes in animals.

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