

demonstrated. We have therefore selectively depleted brain dopamine and noradrenaline by the intraventricular injection of 6-hydroxydopamine in the mouse in order to determine whether or not the behavioural response to GHB can be modified. GHB, at a hypnotic dose, increased the whole brain dopamine concentration and pretreatment with 6-hydroxydopamine 72 h prior to the assay produced a significant decrease in dopamine and noradrenaline concentration (Table 1). GHB did not increase the dopamine concentration in 6-hydroxydopamine-treated animals and, at the same time, the sleeping time (defined as the duration of the loss of righting reflex) was significantly reduced. The GHB sleeping time was not significantly altered in mice pretreated with 4-methyl- α -ethyl-m-tyramine (H75/12), a depletor of brain serotonin (Carlsson, Corrodi, Fuxe & Hokfelt, 1969), at a divided dose of 0.93 mmoles/kg i.p. given at 2 and 4 h prior to the GHB. It is therefore possible that the behavioural effects of GHB are related to its action on dopamine synthesis.

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Effects of central nervous system depressants and stimulants on the acetylcholine concentration of leech ganglia *in vivo*

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Little is known about the effects of drugs on acetylcholine (ACh) metabolism in invertebrate

nervous tissue. Since leech ganglia contain cholinceptive cells (Kerkut & Walker, 1967) as well as ACh, cholinesterase (Cammelli, De Bellis & Nistri, 1974) and choline acetyltransferase (Perkins & Cottrell, 1972), the effects of some centrally acting drugs on the ACh concentration of this preparation were studied.

Leeches (*Hirudo medicinalis*) were placed in beakers containing 100 ml distilled water (controls) or a drug dissolved in distilled water, for 10, 20 or 40 min, after which the ventral nerve cord was rapidly removed. Two cords were pooled as a single sample for the extraction and bioassay of ACh (Cammelli, De Bellis & Nistri, 1974).

Table 1 ACh content of the leech ventral nerve cord

| | ACh (ng/ganglion) | n | Dose | Period of exposure (min) |
|----------|----------------------|----|--------|-----------------------------|
| Controls | 3.09 \pm 0.29 | 11 | — | — |
| Ethanol | 2.91 \pm 0.10 | 4 | 10% | 10 |
| Ethanol | 3.07 \pm 0.66 | 5 | 10% | 20 |
| Leptazol | 1.62 \pm 0.14* | 5 | 10 mM | 10 |
| Eserine | 4.80 \pm 0.35* | 4 | 0.2 mM | 40 |

Mean \pm s.e.m., n = number of experiments; * = $P < 0.01$ when compared with controls.

Exposure to ethanol (10% v/v for 10 to 20 min) 'anaesthetized' the leeches (they became unresponsive to noxious stimuli) without altering the ACh content of the nerve cord (Table 1). Similar results were obtained when the animals were exposed to ether vapour or crushed ice. Leptazol (10 mM/10 min) induced 'convulsions' (strongly increased motor activity) associated with a reduction in the nerve cord ACh levels (Table 1). Eserine (0.2 mM/40 min) produced marked, sustained muscular contractions and an increase in ACh content of the nerve cord (Table 1).

Changes in ACh content in the leech nerve cord were similar to those in the mammalian brain after the administration of stimulant or anticholinesterase drugs (Pepeu & Nistri, 1973). However, during anaesthesia mammalian brain ACh content is increased (Pepeu & Nistri, 1973) whereas in the leech nerve cord there was no change in ACh content.

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Anticonvulsive action of homotaurine and taurine

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The anticonvulsive actions of homotaurine and taurine were tested in cats and rats in comparison with γ -aminobutyric acid (GABA) and glycine. In addition, the cortical levels of taurine and homotaurine were tested, at the end of each experiment, by chromatographic techniques (Guidotti, Badiani & Pepeu, 1972).

Acute midpontine brainstem transected cats were made epileptic: (a) by local application, on

the left and the right sensorimotor cortices, of either cobalt powder (50 mg) or a physostigmine Ringer solution (1.10^{-4}); or (b) by i.v. perfusion of a strychnine sulphate solution (0.5 mg/ml) in curarized cats. The EEG and arterial BP were always recorded.

After the appearance of the epileptic seizures of both cerebral hemispheres, a solution in saline 0.3% of the aminoacid under investigation was slowly (25 mg/min) perfused through the right lingual artery in the circulation of the right cerebral hemisphere.

The appearance of an EEG asymmetry between the right and the left cortices was considered to be the effect of the aminoacid perfusion.

Under these experimental conditions GABA and glycine (up to 1 g) showed no protective

Table 1 Time of convulsion evocation by hyperbaric oxygen

| Rat breed | n | Saline | GABA (370 mg/kg i.p.) three times; once every 12 h | Homotaurine (500 mg/kg i.p.) three times; once every 12 h |
|-------------------|---|--------------------------|---|--|
| | | | | |
| Wistar | 5 | 476 \pm 39* | 620 \pm 52 | 734 \pm 54* |
| Sprague Dalley | 5 | 788 \pm 46** \dagger | 1010 \pm 57** | 927 \pm 22 \dagger |

* $P < 0.01$; ** $P < 0.02$; $\dagger P < 0.05$.

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