controversial issue. DMPE has a potent action on the central nervous system of mice and rats (Brown, Lang & Gershon, 1965; Bueno, Masur, Breda & Carlini, 1969) and cats (Ernst, 1965).

The present study was undertaken to assess the action of this drug when applied iontophoretically, either by itself or in relation to noradrenaline and dopamine, two of the probable neurotransmitters in the brain. DMPE was applied iontophoretically in acute decerebrate, unanaesthetized cats using five barrelled micropipettes according to a technique previously described (Bradley, Dhawan & Wolstencroft, 1966). Of ninety neurones in the region of the medullary reticular formation, DMPE excited three, inhibited eighteen and had no effect on the remainder. These effects were unrelated to the actions of either noradrenaline or dopamine on the same neurone. Prolonged applications of the drug (3–5 min) blocked the inhibitory response to noradrenaline in seven of fifteen neurones tested. In the majority of these neurones this blocking action was partial, although in some cases it was able to block completely noradrenaline induced inhibition. DMPE was ineffective in blocking the excitatory effects of noradrenaline. Of fourteen dopamine responding neurones, DMPE blocked three, of which two were inhibited and one was excited by dopamine. In one case DMPE enhanced the inhibitory action of dopamine.

Our results demonstrate that DMPE is able to interact with two probable transmitters in the brain, thus suggesting a possible neuronal mechanism for its action on the central nervous system.

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Rate of turnover of γ-aminobutyric acid in various brain regions

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The distribution of γ-aminobutyric acid (GABA) in various areas of the brain and the effect of drugs on endogenous GABA levels has been extensively studied (Berl & Waelsch, 1958; Elliott & Van Gelder, 1960; Singh & Malhotra, 1964) but little is known of the dynamic aspects of the metabolism of GABA in the brain. The storage levels of the free amino-acid pool in the brain is not static but reflect dynamic equilibria between the rate of formation and the rates of utilization.

In the present experiments an estimate of the turnover of GABA has been obtained by measuring the rate of disappearance of ^{3}H-GABA from whole brain and from various areas of rat brain after labelling the endogenous GABA pools. It is possible

to use this method to estimate turnover because the brain has a highly efficient uptake mechanism for GABA (Iversen & Neal, 1968) and the ^{3}H-GABA accumulated by the brain parallels the subcellular distribution of endogenous GABA, suggesting that the labelled amino-acid is able to mix uniformly with the endogenous GABA (Neal & Iversen, 1969).

Rats were anaesthetized and ^{3}H-GABA ([2,3-^{3}H]GABA, 20 μCi in 40 μl) was injected into the cisterna magna. After various periods of time the animals were killed and the brains were dissected at 0–4° C. The GABA and acidic metabolites were separated by ion-exchange chromatography.

The disappearance of ^{3}H-GABA from the whole brain was multiphasic and appeared to involve at least two major exponential phases with half times of approximately 0·3 h and 2·4 hours. About 5% of the radioactivity injected remained in the brain after 30 minutes. In the studies on different areas of brain the disappearance of ^{3}H-GABA from the tissue between 2 and 6 h was measured and an estimate was obtained for the half-life of ^{3}H-GABA (Table 1). There were significant differences of turnover in some of the areas studied: the most rapid turnover ((μmol/g)h) occurred in the midbrain and the slowest in the striatum. There did not seem to be any correlation between the rates of disappearance of ^{3}H-GABA from the different areas of brain and the activity of γ-aminobutyrate transferase or the endogenous GABA levels.

TABLE 1. *Rate of disappearance of ^{3}H-GABA from six areas of rat brain*

Brain area	$t_{\frac{1}{2}}$ (h)	95% Confidence limits	Endogenous GABA μmol/g±S.E.M.	Turnover ((μmol/g)/h)	γ-Aminobutyrate transminase ((μmol/kg)/h)
(1) Cerebellum	1·25*	1·00–1·50	1·26±0·089	0·504	11·94±1·02
(2) Pons/medulla	1·92†	1·59–2·25	1·55±0·031	0·405	8·18±1·00‡
(3) Midbrain	2·70	2·42–2·98	3·21±0·063	0·596	8·74 ±1·43
(4) Cerebral cortex/hippocampus	3·24	2·75–3·71	1·82±0·054	0·281	7·22±0·66‡
(5) Striatum	4·70	3·51–5·89	2·39±0·044	0·256	9·84±0·83
(6) Hypothalamus	4·72	4·03–5·31	4·49±0·330	0·475	8·70±1·00

The values of $t_{\frac{1}{2}}$ were calculated from slopes by the formula: $t_{\frac{1}{2}}=(\log_{10} 2)/\text{slope}$. The slopes of different areas were tested for significant differences by applying Student's 't' test to the regression coefficients. Endogenous GABA was measured by an enzymic fluorimetric method (Neal & Iversen, 1969) and γ-aminobutyrate transaminase was determined by the method of Hall & Kravitz (1967). The results are the means of eight experiments.

* Significant difference ($P<0·05$) compared with areas 3, 4, 5 and 6. † Significant difference ($P<0·05$) compared with areas 4, 5 and 6. ‡ Significant difference ($P<0·05$) compared with cerebellum.

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