a table was formed where k_B could be estimated from a single value of m, assuming k_A = 0.29/minute. ACh turnover rate is = k_B[ACh]

m	1.1	1.2	1.5	1.7	2	2.5	3
k_B	1.4	0.88	0.46	0.37	0.27	0.20	0.15

In our drug studies, all the rats were killed at 6 min of infusion. None of the drugs tested changed the steady state of striatal ACh. Apomorphine (4-8-16 μmol/kg) decreased the turnover rate of ACh in a dose related fashion by 20, 40 and 50%, respectively. In the same rats, the turnover rate of striatal ACh was unchanged in the cortex. The inhibition of striatal ACh turnover by apomorphine was completely abolished by pretreating the animals with haloperidol (10 μmol; 1 h before infusion). Dopa (500 μmol/kg 10 min before infusion) decreased the turnover rate in caudate by 50% without any change in the cortex. Haloperidol (10 μmol) increased the turnover rate of striatal ACh, chlorpromazine was less active, clozapine was inactive. The interactions between benztropine and haloperidol were also studied. They suggest that clozapine may be inactive because it blocked the muscarinic receptors. From these studies, it appears that dopamine exerts an inhibitory action in the activity of cholinergic neurones of striatum. Our experiments also suggest that the activity of the striatal cholinergic neurones may have a stimulatory cholinergic input impinging upon a muscarinic receptor.

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Dopaminergic-cholinergic interaction in the striatum: decrease in rat striatal acetylcholine (ACh) levels by dopaminergic and cholinergic antagonists

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We recently reported that pimozide, a powerful neuroleptic dopaminergic antagonist, decreased rat striatal acetylcholine (ACh) levels (Ladinsky, Consolo & Garattini, 1974). Many other drugs have now been found to produce a decrease in rat striatal ACh. The approximate order of potency for the drugs studied were: haloperidol = pimozide $\geqslant$ reserpine $\ggg$ chlorpromazine $\geqslant$ 1-fenfluramine $\geqslant$ clozepine $>$ sulpyrid. Haloperidol (0.5 mg/kg) produced a 50% decrease in striatal ACh 15 min after administration. ACh levels remained markedly reduced 16 h later. The effect of haloperidol on ACh levels in various brain areas demonstrated that when the striatal levels were decreased by 50%, there was only a 17% decrease ($P = 0.05$) in the diencephalon and no effect in the mesencephalon, cerebellum or hemispheric rest after removal of the striatum. Choline levels were significantly decreased in the diencephalon by haloperidol and in the striatum by pimozide.

Striatal choline acetyltransferase and acetylcholinesterase were not affected by these agents after *in vivo* administration or *in vitro* incubation.

The anticholinergic agent, trihexyphenidyl (10 mg/kg) caused a sharp drop in striatal ACh (Consolo, Ladinsky & Garattini, 1974) which was limited only to the striatum and hemispheric rest, there being no effect in the diencephalon, mesencephalon or cerebellum.

It is suggested that the neuroleptics decrease striatal ACh through direct blockade of striatal dopaminergic receptors resulting in disinhibition of striatal cholinergic interneurones and a marked release of ACh. The anticholinergic agent is suggested to produce its effect through blockade of striatal cholinergic receptors resulting in negative feedback of nigro-striatal dopaminergic neurones, causing again, disinhibition of the cholinergic neurones. This would be in agreement with the decreased turnover of cerebral dopamine caused by atropine (Bartholini & Pletscher, 1971) and by trihexyphenidyl (Anden & Bedard, 1971).

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Drug effect on acetylcholine level in discrete brain regions of rats killed by microwave irradiation

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Stavinoha, Peplke & Smith (1970) proposed the use of microwave irradiation for killing small laboratory animals and inducing a rapid and complete heat inactivation of the enzymes involved in acetylcholine (ACh) metabolism. Microwave irradiated brains can also be easily dissected into discrete areas. Relatively few papers are devoted to studies of drug effect on discrete brain areas compared with the large number of investigations carried out on the whole brain (Pepeu & Nistri, 1973).

removed, four areas were dissected out, ACh extracted in an acid medium and quantified by bioassay on the frog rectus abdominis. Choline acetyltransferase (ChAc) was determined by the radiochemical method of Fonnum (1969) in the same areas of a group of control rats killed by decapitation.

The ACh levels are reported in Table 1. They are similar to those reported by Schmidt, Speth, Welsch & Schmidt (1972) by gas chromatographic determination. These results confirm that irradiation gives higher ACh recovery than any previous method of sacrifice.

At the dose used each drug induced a non-uniform change in ACh content. In the frontal cortex which showed the lowest ChAc activity (2.19 ± 0.34 μmol $g^{-1} h^{-1}$) there was no ACh accumulation during pentobarbital anaesthesia but the highest ACh decrease during leptazol convulsions and hyoscine amnesia. The latter drugs

Table 1 Effect of some drugs on ACh (nmol/g ± s.e. mean) levels in discrete brain areas

Drug	*Dose (mg/kg i.p.)*	*Frontal cortex*	*Hippocampus*	*Caudate nucleus*	*Midbrain*
Saline (9)	–	22.78± 2.03	24.49± 1.32	56.30± 0.003	27.46± 1.92
Leptazol (4)	75	8.80±* 2.14	19.15± 2.75	25.53±* 2.09	18.98±** 0.93
Hyoscine (4)	0.5	10.01±* 1.76	18.61± 3.35	42.10±** 4.24	26.19± 4.45
Pentobarbital (4)	35	20.47± 2.42	35.55±** 5.28	78.65±* 3.19	31.86± 2.91

Comparison with saline treated rats: Student t test: * $P < 0.01$; ** $P < 0.02$.

In the present study we have examined the changes in ACh level induced in four different brain areas by some drugs which affect ACh level in the whole brain (Giarman & Pepeu, 1962).

A commercial unit, adapted by Medical Engineering Consultants (Lexington, Mass.), emitting a microwave output of 1350 watts was used for irradiating adult male Wistar rats. Irradiation time was 5 seconds. The brain was then

caused smaller variations in the hippocampus (3.89 ± 0.34 μmol $g^{-1} h^{-1}$) and midbrain (2.92 ± 0.34 μmol $g^{-1} h^{-1}$). In the caudate nucleus a 50% decrease in ACh content after leptazol was found in spite of high ChAc activity (7.62 ± 0.44 μmol $g^{-1} h^{-1}$).

In conclusion the drug induced changes in ACh content in discrete brain areas are not strictly related to the differences in ChAc activity.