In addition, the presence of salicylate has clearly abolished the stabilizing action of the cortisol on the lysosomes.

It would appear that salicylate inhibits the action of cortisol on lysosomes by inhibiting the entry of the steroid into the membrane.

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Effect of eserine injected intraventricularly on behaviour and on activity of cholinesterase in some structures of the cerebral ventricles of the conscious cat

The role of cholinesterase of various brain structures in behavioural changes after intraventricular injection of drugs acting on cholinoceptors is ill-understood. We now report the inhibition of acetylcholinesterase activity in the structures underlying the cerebral ventricles and relate this with the appearance of gross behavioural changes after intraventricular injection of eserine.

Cats of either sex, 1·9–4·4 kg were anaesthetized with pentobarbitone sodium (30–40 mg/kg, i.p.) and a cannula (Feldberg & Sherwood, 1953) was screwed into the skull through which injections were made in conscious cats. Eserine was injected intraventricularly in a volume of 0·2 ml and saline, 0·2 ml, was injected into the cerebral ventricles of controls. Thirty min after injecting eserine or saline the animals were decapitated. Brains were removed and immediately chilled in ice. Acetylcholinesterase activity of slices (Milošević & Andjelković, 1966), 0·5 mm thick, of superficial layers of caudate nucleus, thalamus, anterior and posterior hypothalamus, was measured manometrically in the Warburg apparatus (Umbreit, Burris & Stuffer, 1957). Acetylcholine (0·01 mM, final concentration) was the substrate. Enzyme activity was expressed in μl carbon dioxide liberated per mg of fresh tissue.

By increasing the dose of eserine, the degree of the inhibition of acetylcholinesterase activity was simultaneously increased in the caudate nucleus (Table 1). Acetylcholinesterase activity was inhibited with the highest doses of eserine in the thalamus and hypothalamus.

With a small dose of eserine (0·02 mg), when the acetylcholinesterase activity was inhibited in the hypothalamus, itching and sometimes ataxia developed.

Table 1. *Acetylcholinesterase activity in superficial layers of the caudate nucleus, thalamus, anterior and posterior hypothalamus of conscious cats after intraventricular injections of eserine.* There were six experiments with each dose.

Eserine (mg)	Inhibition (%) in: Caudate nucleus	Thalamus	Hypothalamus anterior	Hypothalamus posterior
0·02	—	—	—	12
0·1	17	—	—	41
0·4	29	—	11	35
1·0	24	—	15	33
2·0	51	44	21	26

But, by increasing the dose of eserine (0·1–1·0 mg), when the symptomatology of autonomic nervous system (mydriasis, hippus, withdrawal of nictitating membrane, piloerection, salivation and lacrimation), akathisia, agitation with signs of fear and anger, rage, increase in depth and rate of respiration and motor disturbances (changes in gait and posture with myoclonic jerks, tremor, athetoid and choreiform hyperkinesias and circling movements) developed, the degree of the inhibition of the acetycholinesterase activity occurred to about the same extent (about 30%) as that in the caudate nucleus and hypothalamus. Moreover, when clonic-tonic convulsions developed after 2 mg of eserine, most of which experiments death occurred within 20 min, the highest degree of inhibition of acetylcholinesterase activity was found in the caudate nucleaus and thalamus.

The results obtained in these experiments indicate that the acetylcholinesterase activity paralleled motor disturbances in the caudate nucleus. With the smallest dose of eserine, motor disturbances have been seldom seen and no changes in the activity of acetylcholinesterase occurred. By increasing the dose of eserine, motor disturbances strengthened and the acetylcholinesterase activity gradually decreased. In the cat, small, unilateral lesions, that damage exclusively the anteroventral region of the caudate nucleus, produce stable and permanent behavioral changes resembling human athetoid and choreiform hyperkinesias (Liles & Davis, 1969). Thus, it is possible that a neurohumoral imbalance produced by a cholinesterase inhibitor can cause motor disturbances mainly originating from the caudate nucleus. Finally, when the inhibition of acetylcholinesterase activity amounted to 50%, clonic tonic convulsions appeared.

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