

LETTER TO THE EDITOR

EFFECT OF CLONIDINE ON ACETYLCHOLINE CONTENT OF RAT BRAIN

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Sir,

A stimulation of central presynaptic α -2 adrenoceptors seems to be involved in anti-hypertensive effects of clonidine, as well as in sedation, it consistently produces in man and in animals (5). Since many sedatives and other depressants are known to alter the brain acetylcholine (ACh) levels (1, 2, 4) it was of interest to study the effect of clonidine on brain ACh content of rats.

Young albino rats (120–190 g) were divided in 4 groups (6 animals per group). One group was injected with clonidine hydrochloride (100 $\mu\text{g}/\text{kg}$, ip); another group received equivalent volume of normal saline only. The third group also received clonidine but was given phenoxybenzamine hydrochloride (10 mg/kg , ip) 1 hr before clonidine injection. The fourth group received phenoxybenzamine hydrochloride (10 mg/kg , ip) alone.

The animals were decapitated 1 hr after various treatments. The brains were excised, weighed and homogenized in ice-cold normal saline containing physostigmine sulphate (15 $\mu\text{g}/\text{ml}$) and cupric chloride (17 $\mu\text{g}/\text{ml}$). Free and bound ACh was extracted by the method of Crossland (2). The ACh content of the extract was estimated (within 24 hrs) using the frog rectus abdominis muscle sensitized with physostigmine (1 $\mu\text{g}/\text{ml}$ of bath fluid), by four-point assay method. The ACh content was expressed as $\mu\text{g}/\text{g}$ of fresh tissue (Table I).

It will be seen that treatment with clonidine caused 27.6% and 42.4% decrease in total and free ACh content of rat brain respectively. This decrease caused by clonidine was significantly antagonized by phenoxybenzamine. Phenoxybenzamine alone did not cause any significant change in ACh content of rat brain.

TABLE I : Effect of clonidine on the acetylcholine content of rat brain and its antagonism by phenoxybenzamine.

Treatment	n =	ACH content ($\mu\text{g/g}$) Free	Mean \pm S.E.M. Total
Normal saline, ip (control)	6	0.59 \pm 0.183	2.75 \pm 1.16
Clonidine HCl (100 $\mu\text{g/kg}$, i p)	6	0.34 \pm 0.143*	2.0 \pm 0.202*
Phenoxybenzamine HCl (10 mg/kg , i p) + clonidine as in (2) after 1 h	6	0.6 \pm 0.24*	2.88 \pm 1.175*
Phenoxybenzamine HCl (10 mg/kg , i p)	6	0.58 \pm 0.616	2.71 \pm 1.18

n = number of animals.

* The value differs significantly ($P < 0.05$, t test) from that of the appropriate control group.

Evidence obtained using blockers of α -2 adrenoceptors (3) shows that sedation due to clonidine involves central presynaptic α -2 adrenoceptors. We have now found that in rats a sedative dose of clonidine also decreases the brain ACh content. Our evidence obtained with phenoxybenzamine indicates that like sedation the change in brain ACh content following clonidine is also mediated through the central α -2 adrenoceptors.

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