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MIBG and Adrenoceptors in Rats

TO THE EDITOR: Iodine-125-metaiodobenzylguanidine has been developed as a tracer of the norepinephrine uptake and storage function in the amine precursor uptake and decarboxylation (APUD) system tumor (*1*) and peripheral adrenergic nerve endings (*2*). We recently showed in vitro that MIBG can also be stored in noradrenergic synaptic vesicles in rat brain (*3*). Since then, it was of high interest to look for MIBG binding on the cerebral adrenoceptors.

Male Wistar rats (15-wk-old) were killed by decapitation and their brains were rapidly removed. Membranes from the cerebral cortex were prepared and binding assayed using a method developed in our laboratory. Binding to alpha 1, alpha 2, and beta-adrenoceptors was measured with hydrogen-3-(^{3}H) prazosin (Amersham, 83 Ci/m*M*), ^{3}H-rauwolscine (Amersham, 91 Ci/m*M*), and ^{3}H-dihydroalprenolol (Amersham, 73 Ci/m*M*), respectively, at Kd concentration. Specific binding was defined as the total bound ^{3}H ligand less the nonspecific binding, determined in the presence of 10 μM of WB4101 (W.B. Chemical Manufacturers) for the alpha 1, guanfacine (Sandoz) for the alpha 2, and propranolol (Sigma) for the beta-adrenoceptors. Membranes (0.7 mg protein/assay) were incubated with ^{3}H ligand and different concentrations of MIBG (CIS-ORIS).

TABLE 1
MIBG Affinity for Adrenoceptors of the Rat Cerebral Cortex

Adrenoceptor	Ligand	IC 50 (n*M*)
alpha 1	^{3}H-prazosin (0.4 n*M*)	1,400
alpha 2	^{3}H-rauwolscine (2 n*M*)	90
beta	^{3}H-dihydroalprenolol (1.3 n*M*)	80,000

Each result is the mean value of four experiments performed in triplicate. IC 50 = concentration of the drug inhibiting 50% of ^{3}H ligand binding (obtained from inhibiting curve).

MIBG interfered with the ^{3}H ligands binding to alpha-adrenoceptors but did not with the ^{3}H-dihydroalprenolol binding to beta-adrenoceptors. MIBG showed a preferential affinity for alpha 2-adrenoceptors bound by ^{3}H-rauwolscine, its corresponding IC 50 value was ~15 times weaker than that for alpha 1-adrenoceptors bound by ^{3}H prazosin (Table 1).

These data suggest that MIBG, which is well known to be a marker of the norepinephrine uptake, is also a marker of alpha 2-adrenoceptors. These receptors are present both on the pre- and post-synaptic side. These findings could have a potential significance in the practical use of MIBG for the scintigraphy of the adrenergic system. In the view of norepinephrine uptake investigation, e.g., in heart diseases, MIBG binding to post-synaptic receptors should be inhibited by an excess of unlabeled alpha 2-adrenoceptors antagonist. Furthermore, MIBG could be useful in the investigation of alpha 2-adrenoceptors, which are suspected to play a role in hypertension (*4*). In this case, MIBG uptake should be inhibited by an excess of unlabeled norepinephrine uptake inhibitor.

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