DIFFERENTIAL EFFECTS OF BENZTROPINE AND DESIPRAMINE ON THE HIGH AFFINITY UPTAKE OF PARATYRAMINE IN SLICES OF THE CAUDATE NUCLEUS AND HYPOTHALAMUS

E. H. PETRALI
Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan, Canada S7N OXO

Accepted September 4, 1979

The effect of benzotropine and desipramine on the uptake of dopamine and p-tyramine was studied in slices of caudate and hypothalamus. In the hypothalamus, of the various combinations of drugs and amines, desipramine inhibited p-tyramine uptake most effectively. In the caudate, benzotropine inhibited dopamine uptake most effectively. It is suggested that in the caudate, p-tyramine may possess its own unique transport system distinct from that utilized by dopamine which is inhibited by benzotropine.

INTRODUCTION

A high-affinity uptake system in the nanomolar range has been demonstrated for both paratyramine (p-TA) and dopamine (DA) in a slice preparation obtained from the caudate nucleus and hypothalamus of the rat (1, 2). Previous reports (3–5) have indicated that p-TA and DA appear to share a common transport system in slice, synaptosomal, and synaptic vesicle preparations. In this paper it is shown that the p-TA and DA high-
affinity transport systems may be differentiated, especially in the caudate nucleus, as a consequence of the effects of benztropine and desipramine.

**EXPERIMENTAL PROCEDURE**

*Preparation and Incubation of Slices*

Slices (0.2 mm) were prepared from caudate nucleus and hypothalamus isolated from rat brain (male Wistar rat, 180–250 g) as previously described (2). Briefly, slices were preincubated (20 min) in Krebs-Henseleit medium at 37°C followed by incubation (5 min) with tritium-labeled substrate in the presence of nialamide (12.5 µM) and ascorbate (1.1 mM). The incubation was terminated by vacuum filtration, and the slices trapped on paper filter disks (Whatman No. 540) were then washed with the medium. Samples without tissue and samples maintained at 0°C were also processed as filter blanks and tissue blanks. Slices were then digested overnight with tissue solubilizer (NCS, Amersham/Searle, Don Mills, Ontario) to which was added liquid scintillation fluid. The amount of radioactivity accumulated (dpm) was corrected for filter blanks and the velocity of uptake calculated as nmol amine/g wet weight/5 min. Uptake values obtained at 0°C were routinely subtracted from those obtained at 37°C.

*Uptake Inhibition by Drugs*

Benztropine and desipramine were included in the preincubation medium and were tested at three different drug concentrations in the high-affinity substrate range (10 nM). ID₅₀ values were calculated by plotting the percent inhibition of uptake velocity against drug concentration using semilogarithmic paper.

[ethyl-1-³H(N)]Dopamine, 8.05 Ci/mmol, and [G-³H]paratyramine, 6 Ci/mmol, were purchased from New England Nuclear, Boston, Massachusetts, and were purified (2) prior to use. Benztropine was obtained from Merck, Sharpe and Dohme, Dorval, Quebec, Canada and desipramine from CIBA-Geigy, Dorval, Quebec, Canada. All other chemicals were of reagent grade.

**RESULTS AND DISCUSSION**

The selectivity of uptake of p-TA and DA in the two brain regions was tested using specific drug inhibitors (6). Table 1 lists the ID₅₀ values obtained from the log probit plots of the percent inhibition of amine uptake by benztropine and desipramine. It can be seen that the most effective inhibition of uptake was that produced by benztropine on DA in the caudate nucleus and by desipramine on p-TA uptake in the hypothalamus. The least effective inhibition was that of desipramine on DA uptake in the caudate nucleus. Desipramine was 14 times more effective in blocking p-TA uptake than DA uptake in the hypothalamus.

Benztropine, although equally effective in blocking p-TA and DA up-