EFFECT OF D-, M-, AND T ANTAGONISTS OF SEROTONIN ON ITS UPTAKE BY HUMAN PLATELETS

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Cocaine, a serotonin M antagonist and dihydroergotamine, a D antagonist, considerably inhibited the uptake of serotonin by human platelets (by 90 and 62% respectively in a concentration of 10^{-4} M). The M antagonist of serotonin, morphine, its D antagonist deseryl*, and the T antagonist tipindole inhibited serotonin uptake by a much lesser degree (by 33, 28, and 18% respectively in a concentration of 10^{-4} M). It is postulated that the "serotonin" center of the membrane carrier participating in the transmembrane transport of serotonin is not identical with any one particular type of serotonin receptor.

KEY WORDS: serotonin; transmembrane transport; antagonists.

Serotonin transport from the synaptic space into the presynaptic ending of the neuron is one of the main methods of intrasynaptic inactivation of the amine [14] and it is, consequently, a possible target for the action of psychotropic drugs [2]. The similarity between the processes of serotonin transport through the presynaptic membrane and through the platelet membrane makes it possible to use the latter as a model with which to study the effect of drugs on transmembrane serotonin transport [9]. This problem is bound up with the function of K^+,Na^+-ATPase and it takes place with the participation of an hypothetical membrane carrier, the centers of which can retain Na^+ and serotonin [11]. Antidepressants of the imiprimine group inhibit serotonin transport into platelets more specifically than neuroleptics, cholinolytics, and amphetamine [4, 13], probably through competition with Na^+ for the centers of the membrane carrier [11] and ATPase [1]. Baumgartner and Born [6] postulated that platelet aggregation induced by serotonin and uptake of serotonin by platelets take place through the binding of serotonin with the same center of the membrane carrier. Serotonin-induced platelet aggregation was prevented by D antagonists, but not by M antagonists of serotonin [8], and it was accordingly concluded that the "serotonin" center of the membrane carrier is identical with the D type of serotonin receptor [8, 11]. However, no reference could be found in the literature that was specially devoted to the investigation of the effect of antagonists of serotonin on its uptake by platelets.

EXPERIMENTAL METHOD

The rate of uptake of serotonin by platelets and the method of statistical analysis of the results were described previously [3]. The substances used and their concentrations are given in Table 1.

EXPERIMENTAL RESULTS

Cocaine and dihydroergotamine, in a concentration of 10^{-4} M, sharply inhibited serotonin uptake by platelets (by 90 and 62% respectively). The effect of morphine, deseryl, and tipindole [5], even in such a high concentration [12], was much weaker (inhibition by 33, 28, and 18% respectively; Table 1). Serotonin antagonists inhibiting its uptake by human platelets thus belong to both the M (cocaine) and D (dihydroergotamine) types, whereas serotonin-induced platelet aggregation was blocked only by D antagonists (LSD-25, dibenzyline, deseryl) [7, 8]. In the present experiments deseryl, which sharply inhibits platelet aggregation [7], caused very little change in the rate of serotonin uptake by platelets, whereas cocaine, which does not affect platelet aggregation [8], clearly inhibited serotonin uptake. Taken as a whole these results do not support the view that

*1-methyl-D-lysergic acid butanolamide.

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TABLE 1. Effect of Antagonists of Serotonin on its Uptake by Platelets (% of inhibition)

Drug	Concentration in incubation medium (in M)*		
	10^{-6} ($n=6$)	10^{-5} ($n=6$)	10^{-4} ($n=6$)
Morphine	18,74±6,51†	28,35±3,22‡	33,17±5,34‡
Cocaine	33,24±5,24‡	62,12±2,34‡	90,05±2,88‡
Deseryl (methysergide)	14,13±6,26†	24,69±5,67‡	28,56±5,79‡
Dihydroergotamine	19,72±3,99‡	24,43±4,56‡	62,33±3,84‡
Tipindole	14,15±6,21†	16,24±4,01†	18,33±2,98‡

*In all concentrations tested the drugs did not change the serotonin concentration in platelets after incubation with plasma for 20 min.
†P > 0.05
‡P < 0.05 compared with control (samples without drugs).

the same "serotonin" center of the membrane carrier is involved in the transmembrane transport of serotonin and in platelet aggregation. The same conclusion was reached by workers who studied the action of deseryl, serotonin, and its derivatives on these two processes [7].

The "serotonin" center of the membrane carrier concerned in serotonin transport is thus evidently not identical with any one type of serotonin receptor (M, D, or T). Inhibition of serotonin uptake by platelets under the influence of cocaine and dihydroergotamine may be the result of the direct action of the drugs on the platelet membrane [10] and not due to their antiserotonin properties.

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