Evidence for a D4 dopamine receptor decreasing serotonin N-acetyltransferase activity in chick retina

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INTRODUCTION. In vertebrate retina melatonin (MEL) level and activity of serotonin N-acetyltransferase (NAT; a key regulatory enzyme in MEL biosynthetic pathway) fluctuate with a light-dependent circadian rhythm, with peak values at night. The nocturnal increase of MEL synthesis is dramatically suppressed by acute exposure of animals to light (1). Experimental evidence suggest that the inhibitory effect of light on the MEL-generating system in retina is mediated, at least partially, by dopamine (DA) acting on D2-like DA receptors (2,3). In this work we verified a subtype of DA receptors regulating NAT activity in the retina of chick.

MATERIAL AND METHOD. Experiments were performed on 2-3 weeks old male white leghorn chicks. The animals were kept from the day of hatching under 12 h light: 12 h dark (LD) lighting schedule. In experiments with D2-like DA receptor agonists, chicks being under a short ether anaesthesia received an intravitreal (i.o.) injection (10 μl/eye, 10 s) of drugs (quinpirole and bromocriptine; right eye) and their vehicles (left eye) at the beginning of the 3rd h of the dark phase of the LD cycle. In another set of experiments D2-like DA receptor antagonists, spiperone and clozapine (10 nmol/eye, each), raclopride and remoxipride (100 nmol/eye, each), were given i.o. 20 min before quinpirole (0.1 mg/kg, ip). The chicks were killed by decapitation 1 h after the administration of the agonists. NAT activity was determined in tissue homogenates by a radioisotopic method (4). Data are expressed as means ±SEM (n=10-12/group) and were analyzed by analysis of variance and Newman-Keuls test.

RESULTS AND DISCUSSION. Of the tested agonists of D2-like DA receptors, i.e. quinpirole (Q; D3/D4 receptor selective) and bromocriptine (B; D2/D3 receptor selective), only Q potently affected NAT activity in chick retina. Q given at doses of 0.1 and 1 nmol/eye significantly decreased the nighttime enzyme activity by 16% and 51%, respectively. Under the same experimental conditions, 1 nmol/eye of B produced only a small (14%) decline in retinal NAT activity (Fig. 1). The Q-induced suppression of the nighttime NAT activity of the chick retina was abolished by spiperone (S; D2-like DA receptor antagonist), and not affected by remoxipride (R; D2 receptor antagonist) (Fig. 2), or by raclopride (D2/D3 receptor antagonist) (data not shown). Interestingly, clozapine (C), an atypical neuroleptic drug with high affinity towards D4 subtype of DA receptors, markedly attenuated the Q action (Fig. 2). The obtained results suggest that DA receptor regulating NAT activity in the retina of chick may represent D4 subtype.

Fig. 1. Effect of D2-like DA receptor agonists quinpirole (Q) and bromocriptine (B) on the nighttime (D) NAT activity in chick retina. *P<0.05 vs. D, **P<0.01 vs. D.

Fig. 2. Effect of D2-like DA receptor antagonists on the quinpirole (Q)-induced suppression of the nighttime (D) NAT activity in chick retina. **P<0.01 vs. Q alone.


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