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# Biphasic effect of the NMDA receptor antagonist MK-801 on the nocturnal NAT activity in chick retina

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**INTRODUCTION AND METHODS.** Serotonin *N*-acetyltransferase (NAT) is a rate-limiting enzyme in melatonin biosynthesis. Its activity (which parallels melatonin levels) follows a diurnal rhythm with high values at night and low values during day-hours of any light-dark illumination cycle (1). In retinas NAT is expressed by photoreceptors (2). Exposure of animals to light at night suppresses the nocturnal enzyme activity, and this effect of light can be mimicked in dark-maintained animals by intravitreal application of retinal neuromodulator dopamine (DA), or selective stimulation of retinal $D_4$-like DA receptors (3,4). Glutamate is a transmitter widely utilized by some types of retinal cells, acting *via* various glutamate receptor subtypes, including the NMDA one (5). Thus, it was of interest to study the effect of NMDA receptors' blockade on NAT induction in the retina. Three-weeks old male white leghorn chicks (kept from the day of hatching under 12 h light:12 h dark illumination cycle) were injected i.p. (under dim-red light) with different doses of a highly selective NMDA antagonist MK-801 ([+]-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine maleate; dizocilpine; RBI) 3.5 h after commencement of the dark phase. The animals, kept still in darkness, were killed 1 h later. NAT activity was assayed as described previously (3). Data represent means ± SEM ($n$ = 5-14/group). Results were evaluated with the aid of ANOVA followed by Student-Newman-Keuls test.

**RESULTS AND DISCUSSION.** Treatment of chicks with MK-801 (0.01-1 mg/kg) produced dose-dependent effects on the night-driven NAT activity in chick retina: a decrease was observed after low doses (0.01 and 0.05), an increase - after 0.25 mg/kg, and again a decrease - after a dose of 1 mg/kg. MK-801 is a highly selective and very potent non-competitive NMDA receptor antagonist (6), and thus the effects reported here seem to result from specific, gradual (dose-dependent) interruption of the retinal glutamatergic neurotransmission between some cells within the retina, especially those receiving an input from photoreceptors and bipolar cells. The physiological meaning of the observation is yet to be established.

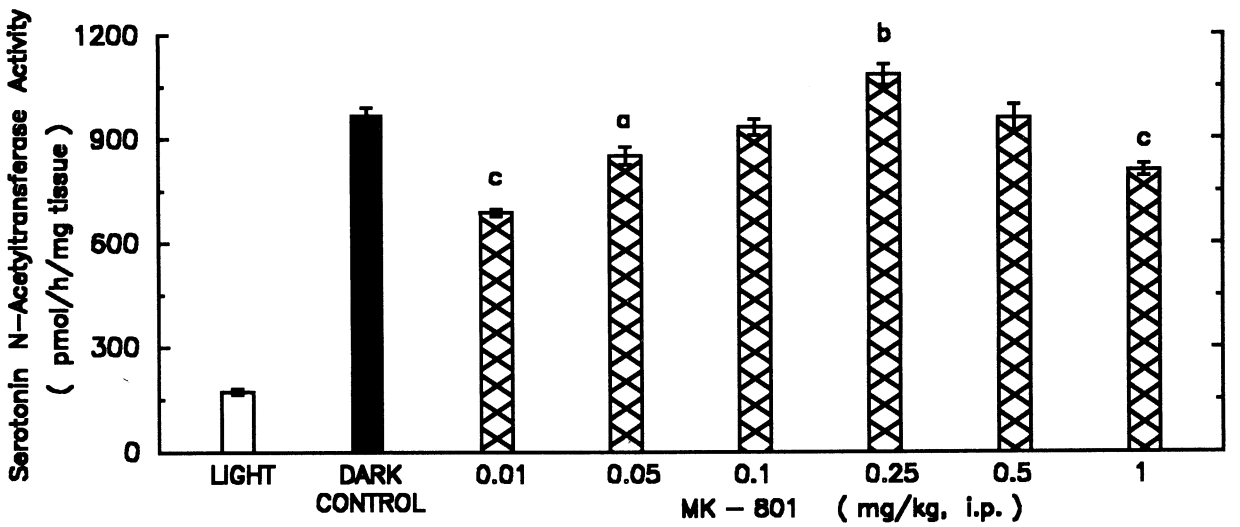


Fig. 1. Effect of MK-801 on nocturnal NAT activity in chick retina. Light represents NAT activity in retinas of birds killed at the end of the light phase of the light-dark cycle. Dark control refers to NAT activity in tissues isolated from chicks injected with saline and sacrificed at approximately the same time as NMDA-treated animals. $^{a}P<0.05$, $^{b}P<0.01$, $^{c}P<0.001$ vs. Dark control.

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