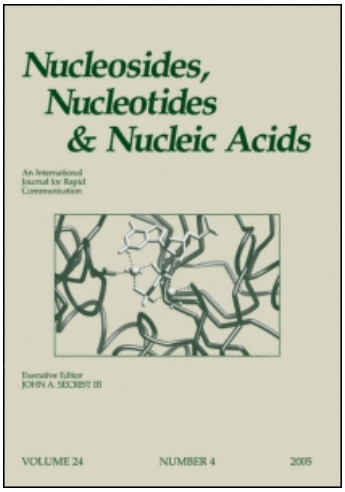

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Circadian Fluctuation in 3H-CHA Binding to Mouse Cerebral Cortex Membranes

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CIRCADIAN FLUCTUATION IN 3H-CHA BINDING TO MOUSE CEREBRAL CORTEX MEMBRANES

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Recent studies indicate that the density of several neurotransmitter receptors is submitted to circadian fluctuation (1). The pharmacological relevancy of these observations derives from the fact that the therapeutic efficacy of drugs may vary according to their administration schedule (2); moreover, also 24-hour rhythms, among which the timing peak of neurotransmitter receptors itself, may be altered by neuroactive drugs (3).

The present study was undertaken in order to ascertain whether adenosine A1 receptors are subdued to diurnal variations. Male mice, exposed for 4 weeks to a 12 hours light/dark cycle (light on at 07.00 hr), were killed at 3-hr intervals across a 24-hr period and crude membrane preparations were obtained from their cerebral cortices. Saturation experiments were performed, using the A1-specific adenosine analog [3H]-cyclohexyladenosine (3H-CHA). Computer-assisted analysis of saturation isotherms (3H-CHA ranging from 0.1 to 10.0 nM) indicated that the density of 3H-CHA labelled binding sites varied throughout the day; the diurnal pattern was characterized by a peak during the dark period, followed by a fall during the light period. The amplitude (defined as peak:nadir per cent) between 03.00 hr (Bmax 0.306±0.01 pmol bound/10 mg wet weight) and 18.00 hr (Bmax 0.230±0.005 pmol bound/10 mg wet weight) was 33%. One way analysis of variance (ANOVA) indicated that the changes were significant ($F=46$, $p<0.005$). No significant difference was found among the Kd values, which ranged from 0.41 to 0.62 nM (mean±SEM of the eight Kd values 0.52±0.07).

Although the physiological relevancy of the timing of A1 cortical receptors remains to be established, a consideration may be advanced. It is widely accepted that endogenous adenosine may act as a natural anticonvulsant (4) and a reduced sensivity to convulsivants has been demonstrated when the cerebral A1 receptors were submitted to up regulation after chronic exposure to the adenosine antagonist theophylline (5); it is thus tempting to correlate the increase of the density of A1 receptors occurring in the cerebral cortex during the night, when the electrocorticogram activity of mice is higher, to the regulation of susceptibility to seizures by adenosine.

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