The Effect of Haloperidol on the Sleep Cycle of the Cat

Haloperidol, a neuroleptic agent whose value in the treatment of psychoses has been established[1], induces marked depressant effects at the level of the central nervous system. Small doses of haloperidol decrease spontaneous motor activity on unanaesthetized animals, increasing the incidence of sleep[2,3].

A number of studies[4,5] have indicated that sleep in mammals is characterized by the cyclic alternation of 2 different phases: (a) sleep with slow-wave activity on the neocortex, high voltage spikes in the hippocampus and a partially relaxed posture, termed slow-wave sleep and (b) sleep characterized by desynchronization of the corticogram, theta activity in the hippocampus, bursts of rapid eye movements (REM) and loss of postural tone, termed REM sleep.

The following experiments have been designed to examine whether various doses of haloperidol may change the rate of cyclic alternation of sleep phases and their electrophysiological manifestations in unanaesthetized cats with indwelling electrodes in the brain.

Electrodes were implanted permanently on the lateral cortex and ventral hippocampus of 5 adult cats, and were also implanted in the dorsal neck muscles for electromyograms and on the outer edges of the 2 orbits for electrooculograms.

Ten days after implantation, when cats were fully recovered, they were placed in a dimly lighted soundproof isolated box which had a one-way mirror. The natural sleep-awake cycle of the animals was recorded in sessions lasting 6 h starting at 09.00.

During the first sessions, the animals' behaviour was affected by the novelty of circumstances. They spent more time awake and it took longer for them to fall asleep and to reach each stage of sleep. There were also more frequent awakenings.

After 4–5 sessions when the animals were fully adapted to their new environment as judged by the consistency of their sleep/wakefulness cycles, treatments were begun.

Haloperidol was dissolved in a 30% aqueous solution of propylene glycol and studied at 3 dose levels (1.0, 2.0 and 4.0 mg/kg) administered in random order. Drug or solvent serving as a control were given at 4 days intervals i.p. 20 min before the experimental sessions began. There were 6 sessions for each cat corresponding with the 3 different drug doses and 3 solvent injections.

After each session we calculated: (a) number of electrographic arousals, (b) total sleep time, (c) percentage slow-wave sleep time, (d) percentage REM sleep time, (e) latency of the first REM period and (f) number of REM periods.

Haloperidol did not induce any appreciable change in the electroencephalographic patterns but significantly modified the sleep/wakefulness cycle. The drug in doses of 2.0 and 4.0 mg/kg significantly delayed the onset of the first REM period and reduced the number of REM periods and the percentage REM sleep time (Table). There was also a significant decrease in the number of awakenings after administration of the highest dose of the compound, most of the wakefulness being at the beginning, after which sleep accounted for almost 100%. Although total sleep time increase was not significant when compared with the control (Table), slow-wave sleep time was significantly increased after 4.0 mg/kg haloperidol.

It is concluded that haloperidol provokes a reduction of REM sleep time and an increase of slow-wave sleep time, although it remains to be determined whether it exercises a potentiation of slow-wave sleep or a specific suppressive effect on REM sleep[6].

The effect of haloperidol on some variables of the sleep-wakefulness cycle

Treatment	No. of arousals	Total sleep time (%)	Slow-wave sleep time (%)	Latency of REM period (min)	No. of REM periods	REM sleep time (%)
Solvent	32.0 ± 6.0	79.9 ± 11.0	54.5 ± 16.6	62.9 ± 23.0	8.8 ± 1.8	25.4 ± 11.1
Haloperidol						
1 mg/kg	22.0 ± 9.0	85.5 ± 9.4	71.2 ± 18.0	103.9 ± 70.5	6.2 ± 3.1[a]	14.3 ± 5.0[a]
2 mg/kg	29.0 ± 4.4	85.8 ± 8.6	79.2 ± 6.7	201.5 ± 65.2[b]	2.6 ± 1.3[b]	6.6 ± 3.6[b]
4 mg/kg	16.0 ± 5.1[b]	92.9 ± 3.7	91.4 ± 5.3[a]	281.6 ± 80.2[a]	1.0 ± 1.0[c]	1.5 ± 3.1[c]

Mean values with standard deviations are shown. Differences in mean values were tested for significance at the 0.05 level by applying the one sample t-test. [a] $P < 0.05$. [b] $P < 0.01$. [c] $P < 0.001$.

Résumé. L'effet de l'halopéridol sur le cycle sommeil/veille a été étudié sur des chats adultes porteurs d'électrodes chroniquement implantées pour l'enregistrement de l'EEG, EMG et des mouvements des yeux. L'halopéridol a fait augmenter d'une manière significative l'indice de sommeil à ondes lentes. Il a produit l'apparition tardive de la première période de mouvements oculaires rapides (REM) en réduisant le nombre de périodes et l'indice du sommeil REM.

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