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Sleep-inducing effects of L-tryptophan

We have demonstrated that L-tryptophan in doses of 4–10 g has hypnotic effects in man. In one study a group of insomniac patients showed significantly increased total sleep, and significantly reduced sleep latency and number of awakenings by behavioural criteria (Hartmann, Chung & Chien, 1971a). In a group of normal subjects (eleven subjects studied over a total of 101 nights) all night eeg recordings showed that L-tryptophan produced significantly shorter sleep latency than placebo; total sleep time and desynchronized sleep time was slightly but not significantly increased (Hartmann, 1970; Hartmann, 1967; Hartmann & others, 1971a). Others have found similar reduction in sleep latency, though there is disagreement about effect on sleep stages (Oswald, Ashcroft & others, 1966; Wyatt, Engleman & others, 1970; Griffiths, Lester & others, 1971).

We have now studied the effects of several dose levels of L-tryptophan on recorded sleep in the rat. All rats were implanted with cortical, hippocampal and with nuchal muscle electrodes and were studied approximately once per week after placebo or after tryptophan feeding over six months, after adaptation to the laboratory.

In a preliminary study with multiple 6–8 h recordings in six animals, tryptophan, 150 and 300 mg, produced little change in waking, or synchronized sleep, and a slight but not significant decrease in desynchronized sleep. Sleep latency could not be accurately measured. Eleven rats with implanted electrodes were in the principal experiment. After adaptation to the laboratory, each received oral placebo on at least three occasions and oral L-tryptophan on three occasions, at doses of 300, 450, and 600 mg/kg in random order. Four of these rats were normals and seven had brain catecholamine concentrations lowered to 40% of normal by a previous injection of 6-hydroxydopamine two weeks before the experiment. (We were interested here in possible interactions between L-tryptophan and the catecholamines.) Rats were studied for on 8 h recording every week for four months. Results are in Table 1. L-Tryptophan produced a dose-dependent reduction in sleep latency in both groups of animals. There was no significant change in amount of time spent in waking, synchronized sleep or desynchronized sleep and there was no difference in the number of awakenings. The cycling or architecture of sleep was relatively normal. There was no clear interaction between 6-hydroxydopamine and L-tryptophan. (The effects of 6-hydroxydopamine itself on sleep have been discussed elsewhere (Hartmann, Chung & others, 1971).

Table 1. *Effect of L-tryptophan on sleep in the rat.*

Tryptophan dose (mg/kg)	W (min)	S (min)	D (min)	Number of awakenings	Sleep latency
		Control (saline) animals (N = 4)			
0	167·0 ± 17·5 33·4 ± 3·3	266·0 ± 10·4 55·1 ± 7·7	48·4 ± 6·4 10·1 ± 1·7	37·8 ± 2·3	12·9 ± 3·0
300	140·0 ± 39·0 29·1 ± 8·3	295·0 ± 28·0 61·4 ± 5·6	45·7 ± 14·7 9·3 ± 2·9	29·3 ± 6·9	9·8 ± 5·1
450	204·0 ± 43·0 40·7 ± 8·1	260·0 ± 38·1 54·6 ± 7·5	22·4 ± 7·5 4·8 ± 1·6	38·0 ± 6·0	4·2 ± 0·8*
600	175·0 ± 19·0 36·4 ± 4·0	264·0 ± 21·8 54·9 ± 4·5	41·5 ± 2·8 8·7 ± 0·6	41·3 ± 3·7	5·8 ± 4·0*
		6-Hydroxydopamine-treated animals (N = 7)			
0	143·0 ± 4·7 29·8 ± 1·0	268·7 ± 5·7 55·8 ± 1·2	69·7 ± 6·2 14·5 ± 1·0	45·5 ± 2·2	10·1 ± 2·4
300	148·5 ± 29·6 31·0 ± 6·2	277·0 ± 22·1 57·9 ± 5·1	53·5 ± 10·6 11·1 ± 2·2	42·7 ± 5·1	6·9 ± 1·9
450	121·5 ± 18·6 25·4 ± 3·8	294·5 ± 10·8 61·5 ± 2·2	62·4 ± 7·8 13·2 ± 1·6	28·8 ± 2·6	4·2 ± 1·4*
600	200·0 ± 69·2	241·0 ± 56·5	36·5 ± 13·0	46·5 ± 7·5	2·8 ± 2·7*

* Different from control (no tryptophan) condition $P < 0{\cdot}01$ (two-tailed).

8-h recordings were conducted on 11 rats for a total of 54 recordings over four-months. The values represent the mean plus or minus the standard error of the mean of 8-h recordings at each dose. W = waking; s = synchronized sleep; D = desynchronized sleep.

Thus in the rat as well as in man, the amino acid L-tryptophan can produce significant decreases in sleep latency with little change in sleep architecture. This differentiates tryptophan from most clinical hypnotics, which distort sleep architecture considerably.

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