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The Insomnia of 'Sleeping in a Strange Place': Effects of *l*-Tryptophane

ERNEST HARTMANN and RICHARD ELION

Tufts University and Boston State Hospital, 591 Morton Street, Boston, Massachusetts 02124, U.S.A.

Abstract. Forty-two normal human subjects were studied in the sleep laboratory for one night each. Fourteen were given placebo at bedtime, 14 took *l*-tryptophane 1 g, and 14 took *l*-tryptophane 3 g. Both tryptophane groups had significantly lower sleep latency than the placebo group. The usually discarded 'first laboratory night' produces a mild situational insomnia in normal persons and thus can be useful in certain sleep studies.

Key words: Sleep – Sleep latency – Insomnia – D-sleep (desynchronized sleep) – *l*-Tryptophane

In most laboratory sleep studies the first one or two nights of sleep are routinely discarded as 'adaptation' nights. However, the first night in the laboratory produces in many subjects a mild insomnia – the insomnia usually associated with 'sleeping in a strange place' – that might be useful in testing hypnotic effects of a chemical or drug in normal subjects. As determined by use of standard methodology, normal persons often have sleep latencies and waking times close to zero after adaptation, which makes any reduction impossible to detect. We found that these same normal subjects usually take at least 10–15 min to fall asleep when they first sleep in the laboratory. In this study we employed a relatively large number of subjects who each slept in the laboratory one night to investigate the effects on sleep of the amino acid *l*-tryptophane.

We previously demonstrated that at doses of 450 mg/kg and 600 mg/kg *l*-tryptophane significantly reduces sleep latency in the rat (Hartmann and Chung, 1972) and that doses of 5–10 g at bedtime significantly reduce sleep latency in normal human subjects (Hartmann et al., 1971). We recently demonstrated that in a group of mild insomniacs (sleep latency over 30 min) a dose of *l*-tryptophane as low as 1 g significantly reduced sleep latency. Dosage levels of 1–5 g produced no change in sleep stage patterns, while 10 or 15 g did produce some minor changes (Hartmann et al., 1974). We investigate here the effects of 1-g and 3-g doses on laboratory-recorded sleep.

METHODS

The subjects were 42 normal young male and female college students between 19 and 23 years of age. They were screened for medical normality using a brief interview and the Cornell Index. None were taking medication and all were naive to the sleep laboratory. Subjects were assigned to one of three groups matched as closely as possible for age, sex distribution, reported sleep latency at home, reported sleep length at home, and reported use of alcohol and marijuana (Table 1). Each subject took six white tablets 20 min before bedtime. One group received six placebo tablets; the second group received two 500 mg tryptophane tablets and four placebo tablets; and the third took six 500 mg tryptophane tablets. The subjects, the technician who ran the recordings at nights, and the experimenter scoring the records were all blind as to treatment condition.

The usual electrodes were attached to record parietal and occipital EEG, electro-oculogram, and submental EMG. All-night records were made on a Grass model VIII EEG at 10/mm/s and were scored for stages of sleep according to the usual sleep laboratory criteria (Rechtschaffen and Kales, 1968).

RESULTS

Table 2 presents the results for the three groups. Figure 1 presents individual values for sleep latencies. Sleep latency was significantly lower in both tryptophane groups than in the placebo group. No other changes were significant (using one-way Anova followed by *t*-tests for individual contrasts). There were no significant differences between the two doses of tryptophane. There was a trend toward more total sleep time with 3 g of tryptophane, compared to 1 g or to placebo. When all tryptophane subjects ($N = 28$)

Table 1. Characteristics of the three groups

	Group A (placebo)	Group B (trypto-phane 1 g)	Group C (trypto-phane 3 g)
Sex	9 M, 5 F	10 M, 4 F	9 M, 5 F
Median age	19	19	19
Mean reported sleep latency at home (min)	12.5	15.4	12.1
Reported total sleep time at home (h)	7.7	7.7	8.0

Table 2. Sleep laboratory results

	Placebo ($N = 14$)	Tryptophane 1 g ($N = 14$)	Tryptophane 3 g ($N = 14$)
Sleep latency (min)	24 ± 6.9	14 ± 2.7*	15 ± 2.9*
Total waking (min)	34 ± 6.9	28 ± 6.6	28 ± 6.2
Total sleep (min)	342 ± 10.8	346 ± 12.6	358 ± 17.3
D-time (min)	72 ± 7.6	64 ± 6.0	73 ± 10.2
Stage 1 (min)	16 ± 3.3	14 ± 2.3	17 ± 3.9
Stage 2 (min)	136 ± 9.1	150 ± 9.8	151 ± 11.2
Stage 3 (min)	42 ± 6.6	35 ± 5.4	33 ± 4.0
Stage 4 (min)	78 ± 8.0	83 ± 4.8	84 ± 5.3
Number of D-periods	3.6 ± 0.46	4.4 ± 0.25	4.6 ± 0.38
D-latency (min)	137 ± 13.6	114 ± 10.3	113 ± 10.5

Values are means ± SEM for 14 subjects; * $P < 0.05$, two-tailed

were compared with all placebo subjects ($N = 14$) (a planned comparison), tryptophane subjects had a lower sleep latency ($P < 0.005$), a lower D-latency ($P < 0.05$), and more D-periods ($P < 0.05$).

Since sleep latency scores do not form a normal distribution but are nearly always skewed to the right, we also examined median values and ranges. The placebo group had a median sleep latency of 20 min with a range of from 3 to 102. For tryptophane 1 g, the values were 12, and 4 to 37. For tryptophane 3 g, 11.5 and 3 to 38. Differences were significant using the Mann-Whitney U test.

DISCUSSION

It is clear that low doses of *l*-tryptophane produce a reduction in sleep latency. It is of interest that here, as in two of our other studies (Hartmann et al., 1974; Davis et al., 1975) *l*-tryptophane appears to reduce or eliminate the very high sleep latencies, for in this study 2 of the 14 placebo subjects had latencies greater

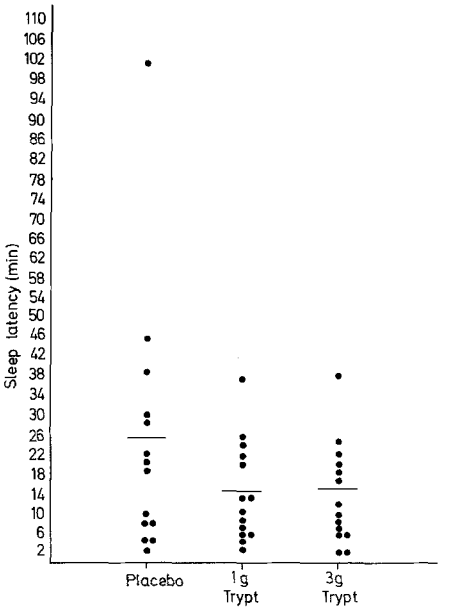

Fig. 1. Individual values for sleep latency

than 45 min, while the highest latency among the 28 tryptophane subjects was 38 min. As in our other studies, we find here that *l*-tryptophane in low doses does not alter the stages and cycles of sleep.

It appears that the present methodology may be useful in the study of hypnotic medication. A larger number of subjects than usual can be studied at less expense, and 'sleeping in a strange place' may closely resemble situations in which mild over-the-counter hypnotics are actually used.

We have now used *l*-tryptophane clinically in 25 insomniac patients in addition to the 200 subjects and patients treated in our research studies. Our impression is that *l*-tryptophane, as could be expected, is not a 'powerful' drug that can be used to calm a severely agitated patient. It produces an ordinary sort of drowsiness faster than placebo (Hartmann et al., 1976) and induces sleep faster than placebo. It could have a clinical role in treating mild or moderate sleep-onset insomnia.

Further study of long-term administration of *l*-tryptophane is required for the sake of both safety and efficacy. We have shown in small-scale studies (Hartmann and Cravens, 1975) that 28 days of *l*-tryptophane administration (1 g or 4 g nightly) does not produce distortion of sleep stage patterns either during administration or after discontinuation, and the use of 6 to 9 g of *l*-tryptophane daily over many months for the treatment of depression without serious side effects (Coppen, Cambrian Chemicals Ltd. and Medicines Council of Great Britain: personal communication) suggests that *l*-tryptophane is a relatively safe drug.

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