L-Tryptophan and D, L-5-Hydroxytryptophan Effects on Sleep of Chronic Schizophrenic Patients

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Tryptophan and 5-hydroxytryptophan (5-HTP), amino acid precursors of serotonin, have been shown to be capable of modifying the sleep pattern of normal subjects. Results obtained with tryptophan are contradictory [Oswald et al. 1966; Hartmann, 1967; Williams et al., 1969; Wyatt et al., 1970], but an increase in stage rapid eye movements (REM) has often been reported, especially with higher dosages [Williams, 1971]; there is, however, substantial agreement for an increase in REM sleep with 5-HTP [Mandell et al, 1964; Oswald et al., 1966; Wyatt et al., 1971]. These data seem, in part, to conflict with those obtained with laboratory animals in which there has been observed an effect of 5-HTP upon NREM (non REM) sleep [Jouvet, 1969].

It was considered to be of interest to investigate a possible modification by the two precursors upon the sleep pattern of schizophrenic subjects in view of the hypothesis of an altered metabolism of serotonin in schizophrenic syndromes.
A group of 6 male chronic schizophrenics with a sleep pattern essentially characterized by a substantial reduction of stage 4 sleep was used for the present study.

The subjects formed a group homogeneous in age (average age 41.3 years), duration of illness and symptomatology at time of the investigation.

After a placebo period lasting at least 30 days, L-tryptophan, mixed with applepulp, in doses of 100 mg/kg/day was given for a period of 4 days. After 60 days of placebo d,l-5-HTP was administered in fixed doses of 500 mg/days, in capsules, for 3 days. Tryptophan and 5-HTP were given 15 min before retiring, taking into account the absorption time of the compounds [Oswald et al., 1966]. The subjects were on a tryptophan-poor diet.

Tryptophan and 5-HTP (table I) had no effect on sleep time but increased stage REM. Tryptophan reduced REM latency, and sometimes REM sleep began immediately with sleep onset; 5-HTP reduced S-sleep (stages 3 and 4) on the last day.

After withdrawal of the two amino acids the sleep pattern returned to baseline values.

The modification of sleep and, in particular, the increase in stage REM observed with tryptophan (tryptophan vs. placebo) and 5-HTP (5-HTP vs. placebo) are not results which are statistically significant (Student’s t-test).

In both cases, half of the subjects responded in a similar way while in the rest there were irregular variations. This may be due to the doses used and/or the short period of observation. It is also possible that the group of patients, homogeneous with respect to symptomatology, was fundamentally heterogeneous since it is recognized that the schizophrenic syndrome in different individuals may be due to different etiopathogenic factors.

A statistical comparison of the effects of tryptophan and 5-HTP at corresponding times (table I) does not show significant differences between the two precursors except for a reduction of S-sleep on the last day of the administration of 5-HTP.

Thus, the similarity of action of tryptophan and 5-HTP on REM sleep suggests that both compounds may give rise to the metabolic by-products
or to an increase of serotonin in serotoninergic brain areas, capable of modifying REM sleep.

In conclusion, these results and the data of Zarcone et al. [1971] in two schizophrenic children demonstrate that tryptophan and especially 5-HTP provoke changes in REM sleep of chronic schizophrenics which are similar to those found in normal subjects.

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References


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Influence of Melatonin on Sleep in Humans

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Melatonin (5-methoxy-N-acetyl-tryptamine) was isolated and identified by Lerner [6]. In mammals, this indole hormone is almost exclusively manufactured in the pineal gland. Melatonin exerts a depressant action on several endocrine glands, such as the gonads and thyroid, but specific physiological roles of this indole amine are unknown. The activity of hydroxyindole-O-methyltransferase, the melatonin-forming enzyme in the pineal,