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A Proposed Mechanism for the Visions of Dream Sleep

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Abstract — The visions of dream sleep are suggested to occur through a dream mechanism which implicates tryptamine derivatives as endogenous paychedelics. The hallucinations that occur in some schizophrenic syndromes are also proposed to occur through a similar, though desynchronized, mechanism. These compounds occur in the human pineal gland and are regarded as neurotransmitters or neuroregulators. A protocol for experimental verification is suggested.

Introduction

Much has been written concerning various states of consciousness precipitated with and without the assistance of drugs, though most of the scientific literature distances itself from the psychedelic experience by suggesting it as a model of induced psychosis (i.e., psychotomimetic) or other undesirable state of mind. Few have considered this experience as a normal occurrence (12). However, it has been suggested that the human urge to deliberately alter consciousness is as innate as any natural drive (35). This idea is extended by the suggestion that through dreams the mind experiences alternative states of consciousness on a regular basis, and gains perspective and insight into waking reality. Dream phenomena are transcultural, predate literature and occur in virtually all humans (and perhaps other animals) several times a night. Yet dreams are perhaps the least understood facet of human experience.

Humans spend approximately one third of their lives asleep. During this period of rest and rejuvenation, less than one fourth of the time is spent in the dream state commonly referred to as rapid-eye-movement (REM) sleep, or REMS. REMS is the last of five qualitatively different stages of sleep that can be characterized by electroencephlographic activity. Although the correlation between REMS and dream sleep is strong it is not absolute. (For reviews of dream sleep see references 7 and 14). The REM stage usually increases in length during the sleep cycle, often reaching a period of approximately two hours prior to waking. Dreams also increase in length and intensity throughout the sleep cycle. The most vivid and emotionally charged dreams also tend to occur just prior to waking. These are the dreams best remembered in the waking phase of ths human circadian cycle.

This article suggests an outline of a dreaming mechanism and cites endogenous compounds

that possibly play a role in REMS, and more specifically, the visual phenomenon of lucid dreaming. Such compounds could also account for other alternative states of consciousness, such as experienced in certain meditative practices, and might be psychedelic when administered during the waking phase. They must be produced endogenously during sleep, with their dream-inducing qualities being dose dependent and relatively short acting (15 minutes to two hours). Dose dependency is indicated by the gradual increase of REM activity throughout the sleep phase, when most of the neurotransmitters are produced to sustain longer episodes of REMS. In as much as humans dream periodically, these compounds would also be involved in a mechanism of dream initiation/inhibition to start and stop the dream process. In this way the dream state does not dominate the sleep phase and allows for a certain amount of vigilance to be maintained. Though some overlap may be necessary for normal "day dreaming", excessive seepage may occur into the waking phase without such a periodic regulatory mechanism. Such an overlap may occur in some schizophrenic patients, where a desynchronized dream mechanism allows the intrusion of dream chemicals into the waking state (20). Such chemicals have been proposed in the transmethylation hypothesis (26). Rather than limiting this mechanism to abnormal behavior, the transmethylation of specific endogenous compounds during sleep may actually be an important part of normal mental health within a properly functioning dream mechanism, and not merely the harbinger of mental disease. beta-Carbolines and tryptamines are two classes of compounds implicated in this balance of dreaming and insanity.

beta-Carbolines (harmala alkaloids) are alkaloids found in many plants and animals. They are thought to occur in humans as condensation products of indolealkylamines (tryptamines) with aldehydes (formaldehyde), formed through enzymatic reactions with 5-methyltetrahydrofolate (5-MTHF) and/or S-adenosyl-l-methionine (SAM), and catalyzed by N-methyltransferase (NMT) (1, 6, 10, 30, 34). This condensation is followed by a less understood cyclization. In addition, beta-carbolines have been proposed as endogenous ligands to the so called benzodiazepine receptor (19, 23), suggesting a link to anxiety release and control.

Some of the beta-carbolines have demonstrated psychoactive properties in humans when taken in their pure form (32), but are qualitatively different in their effects from LSD or mescaline. Naranjo (24, 25) stated that distortion of form, depth-movement perception and color enhancement were not observed in a series of beta-carbolines. The most frequently occurring phenomena included, "superimposition of images on flat surfaces and viewing scenes simultaneously with an undistorted perception of surrounding objects". Abundant bright and vivid colors were reported with eyes closed. According to Naranjo (25) the characteristic effects of 6-methoxy-beta-carbolines were considered, "to be of a less hallucinogenic nature . . . being more akin to a state of inspiration and heightened introspection."

Naranjo (25) also noted a recurrent visual phenomena of, "rapid lateral vibration in the vision field." Harmaline has been found to produce a generalized tremor at a frequency of eight-12 Hz in many animals (10). This same band of frequencies has been designated as alpha brain waves in humans. These waves occur normally when the eyes are closed in a waking state and during REMS, but not during the other four stages of sleep (7). The harmaline induced vibratory phenomenon of the visual field is interesting in the context of REMS, where the rapid eye movements echo a deeper process in sleep. Anthropological data suggest that harmala alkaloids (beta-carbolines) may be more than merely hallucinogenic in actual usage. These compounds have traditionally been used in preliterate societies to produce out-of-body experiences clairvoyance, simultaneous group visions, remote viewing and divination (15, 24).

About 10 different beta-carbolines have been found in mammalian tissue (1). Although their metabolic precursors are naturally available, the exact in vivo biosynthetic pathways involved have yet to be definitively established. Water soluble metabolites of endogenously produced beta-carbolines have been identified in human urine and there is increasing evidence to suggest that some of these compounds are formed under special physiological circumstances, such as after alcohol consumption and perhaps at other times (1, 2, 28, 34). beta-Carbolines are found in human plasma and are highly concentrated in platelets (33). 6-Methoxytetrahydro-beta-carboline, also called 6-methoxytetrahydronorharman, has been found in the human pineal gland (29) and retina (16), possibly acting as a neuromodulator or neurotransmitter, and has been

named pinoline. Like most beta-carbolines, pinoline is a typical serotonergic compound, a property shared with psilocybin and other psychedelic tryptamines. It inhibits the enzyme monoamine oxidase-A (MAO-A) and has the unique property of increasing concentrations of brain serotonin (10). Since pinoline and other endogenous beta-Carbolines inhibit MAO-A, they can competitively inhibit that enzyme while other psychoactive but metabolically more labile compounds, such as tryptamines, act centrally to promote the visions of dreams. A synergistic relationship between ingested tryptamines and beta-carbolines has been auggested (21, 22). Dimethyltryptamines have not been definitively established to occur endogenously in humans, though the in vitro evidence is highly suggestive (4, 5, 31). This lack of confirmation is not surprising when one considers the minute concentrations involved, sensitivity of detection methods and instability of endogenous tryptamines (11). (See reference 31 for a review of endogenous paychedelics). The time of sampling during the circadian cycle may also be crucial in detecting psychodynamic tryptamines (18).

During the sleep phase, melatonin is derived from serotonin, which is in turn metabolized from the amino acid tryptophan. 5-Methoxydimethyltryptamine and DMT, both potent psychedelics, have also been proposed by Barker (5) to derive from tryptophan through SAM and NMT (see Fig. 1). Melatonin, like serotonin, is produced primarily in the pineal gland. Its generation seems to be inhibited by light entering the eye (3, 8, 18). Generation of melatonin may begin soon after the eyes have closed, as in the onset of sleep and perhaps in some meditative states. During the sleep cycle of most animals studied, including humans, the levels of serotonin decreased while the levels of melatonin increased (18). According to Ebihara (8), this decrease in serotonin is partly due to its transformation to melatonin (see Fig. 2). Endogenous beta-Carbolines are also proposed to derive from serotonin through the increased activity of NMT and 5-hydroxyindole-0-methyltransferase (5-HIOMT), both pineal enzymes of the sleep phase (1, 6, 10). Pinoline and melatonin were found to occur in nearly similar concentrations in the human retina. The origin of retinal pinoline seemed to be mostly pineal, with only a fraction being locally synthesized (17). All of the chemical structures shown in Figure 2 have been identified in the human pineal. The intermediate structure in brackets is one of two proposed by Ho (10). The solid arrows denote pathways which are known to occur in vivo, while the broken arrows have only so far been demonstrated to occur in vitro.

Figure 3 represents a proposed dream cycle. As melatonin production increases in the sleep phase, the brain descends through the four stages of sleep. beta-Carbolines and dimethyltryptamines are derived from tryptamine, and when enough are produced, the mind enters dream sleep. This is reflected by the brain as

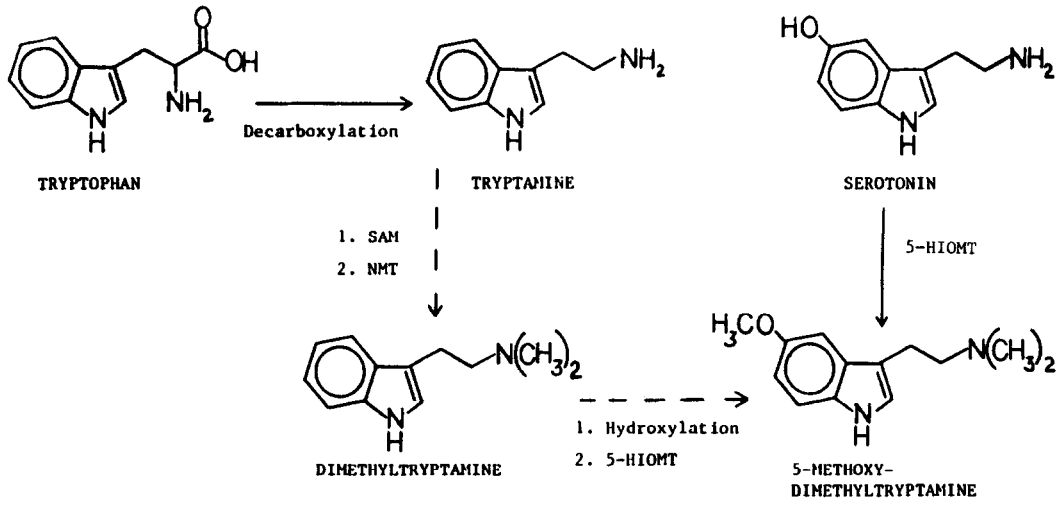

Figure 1

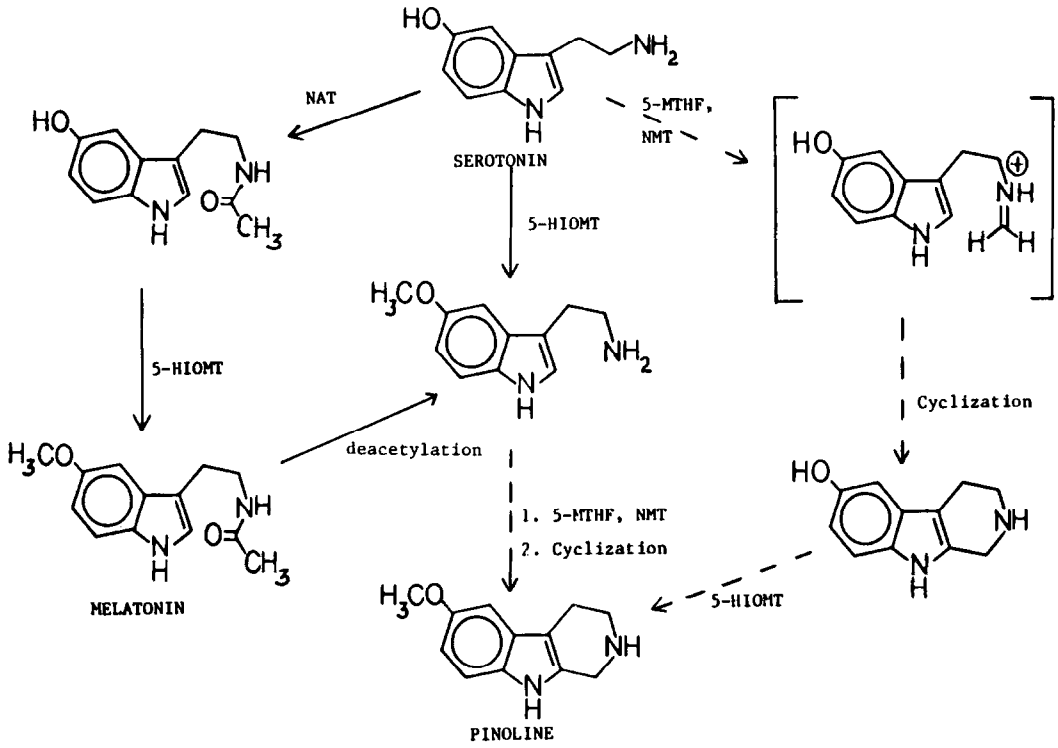

Figure 2

REMS. Pinoline increases brain serotonin levels, especially at low concentrations (2, 10, 33), which eventually inhibits dream sleep by taking the brain back through the four sleep stages. Before the cycle reaches the waking phase, N-acetyltransferase (NAT), NMT and 5-HIOMT work to metabolize the excess serotonin to melatonin, pinoline and perhaps other tryptamine derivatives. The cycle then repeats and its period lengthens throughout the night. The longest and best remembered dreams occur just prior to waking from the cumulative concentrations of psychoactive tryptamine derivatives which have become active through progressive inhibition of MAO-A by pinoline and/or other beta-Carbolines. Other circadian mechanisms come into play before waking so that the dream cycle does not overlap into waking consciousness. It is not unlikely that beta-Carbolines and/or other tryptamine derivatives act centrally to induce the visions of dreams. Although Ho (10) was speaking in terms of psychosis, the following applies with few modifications, "It is quite possible that a psychotic state could result from a shunt of serotonin metabolism to a pathway that occurs and leads to accumulations of abnormal amounts of such potentially psychotomimetic compounds."

This dream cycle hypothesis could be tested in a couple of experiments. One would be to monitor the serum and/or cerebral spinal fluid levels of beta-Carbolines throughout the circadian cycle, with expectations of higher concentrations during sleep and the REM stages of sleep. A more ambitious procedure would be to determine beta-Carboline levels in normal and schizophrenic subjects before, during and after REMS deprivation. When normal individuals are deprived of REMS, a rebound of REM activity occurs in subsequent nights of undisturbed sleep. Schizophrenics show no such rebound. Therefore one might expect to see elevated beta-Carboline levels during rebound in normals, with schizophrenics maintaining their normal predeprivation levels. Morning levels of pinoline in normal and schizophrenic patients were found to be equivalent after normal sleep (29). Animal studies suggest that pineal levels of pinoline and melatonin are of the same order and change in concert during the circadian cycle (13). Mela-

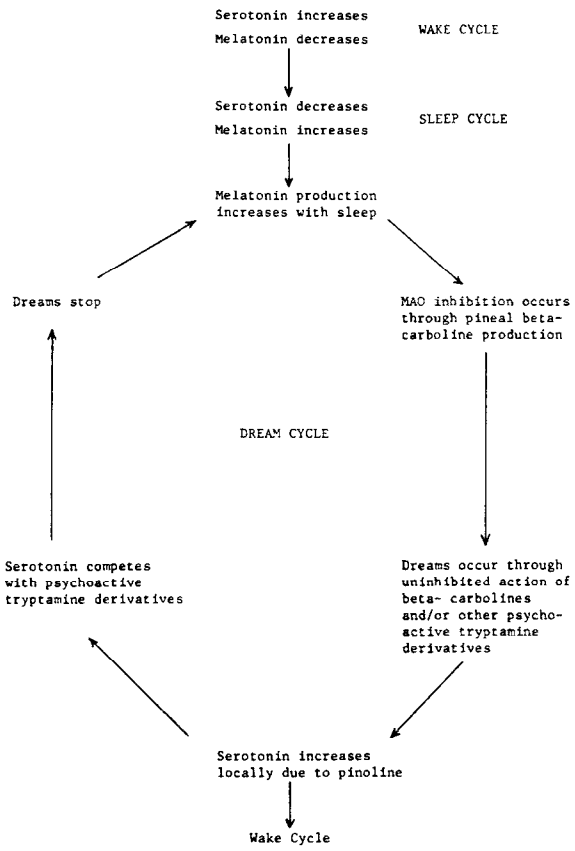

Figure 3

tonin administered before sleep decreases the time of sleep onset and increases the incidents of vivid and colored dreams (27), and could serve as a precursor to psychoactive beta-Carbolines.

It should be mentioned that this hypothesis is not the currently accepted view of a mechanism for REM-dream sleep. In a recent article (9), acetylcholine was the neurotransmitter implicated as being responsible for initiating and maintaining REMS. It is quite likely that acetylcholine, along with several other neurotransmitters, plays a major role in REMS, yet the actual catalyst for the dream state itself may be quite different in nature and function than the transmitters involved in the physiology of REMS.

Conclusion

This article speculates on the endogenous production of psychedelic compounds to account for dream phenomena through a metabolic dream cycle, and posits that such a mechanism may be discrete from the physiological symptomatology observed in the rapid eye movements of REMS. With tryptamines and beta-Carbolines proposed as a search targets, it may eventually become possible to find "the kind of stuff that dreams are made on."

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