Dreams, Hallucinogenic Drug States, and Schizophrenia: A Psychological and Biological Comparison

by Lawrence G. Fischman

Abstract

Many observers have noted similarities between dreams, hallucinogenic drug states, and schizophrenia. In the present article, certain fundamental areas of convergence between the three states are described. Consideration is given to the hallucinogenic drug model of psychosis: the reasons for its initial attractiveness, and the reasons for its current disfavor. The concept of ego boundaries is defined, examined, and applied to the three states. In these states, the ego's capacity to average or synthesize various self-representations into a continuous, coherent self is compromised—leading to an impairment of the reality-oriented secondary process, and the emergence of the florid attributes of the primary process. This can account for many of the familiar characteristics of the three states. Current neurophysiological theories of dream and hallucinogenic drug states are presented, with emphasis upon serotonin neurotransmission. Serotonin appears to play a prominent role in the regulation of these states. The analogy contained in the present article suggests that serotonin may play a role in regulating schizophrenic states as well.

The similarity between dreams and madness has been noted frequently throughout recorded history, ever since phenomenological observations to this effect were made by Aristotle and Plato (see review by Evans 1962). Kant stated, "The lunatic is a wakeful dreamer." Schopenhauer wrote, "A dream is a short-lasting psychosis, and a psychosis is a long-lasting dream."1 Freud simply remarked, "A dream, then, is a psychosis" (Freud 1940, p. 172).

In the mid-nineteenth century, Moreau (de Tours) added a new dimension to this analogy. Moreau (1845) suggested that hashish-derived hallucinations and mental illness were virtually identical psychical states resulting from cerebral excitation; that the ingestion of hashish brings about a kind of "sleepless dream" (p. 19). Moreau was thus the first to note the phenomenological similarities between the three states of consciousness to be discussed here: dreams, drug-induced states, and psychosis.

With Hoffman's (1979, p. 58) serendipitous discovery of the "dream-like" effects of d-lysergic acid diethylamide (LSD) a broad-based research effort was undertaken to elucidate the biological and psychological mechanisms of hallucinogenic drugs, in the hope that such knowledge would lead to an understanding of the basis of schizophrenia. In another arena, the discovery of rapid eye movement (REM) sleep epochs (Aserinsky and Kleitman 1953) precipitated an intensive investigation into the physiology of sleep and dreams. The purpose of this article is to show that recent advances in the fields of neurophysiology, psychopharmacology, ego psychology, and behavior can be related to the observations of Moreau and others in demonstrating similarities between dreams, hallucinogenic drug states, and psychosis. No claim is made here for identity between these states. The three states share several common properties, but each of the three retains an identify-

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1 The translated quotations of Kant and Schopenhauer are from La Barre (1975, p. 12).

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A Chemical Psychosis?

Kraepelin was the first to attempt a systematic study of the phenomenology of mental illness by means of chemically induced psychoses, but as Knaur and Maloney (1913) attest, the substances employed by Kraepelin produced syndromes which bore little resemblance to endogenous psychosis. Knaur and Maloney were the first to utilize one of the substances variously called “psychedelics,” “hallucinogenic,” or “psycho-tomimetic”—namely, mescaline—as a model for insanity. Beringer (1927) was credited with the application of the term “model psychosis” to the mescaline-induced state. His study was followed by those of Kluver (1928), DeJong (1930), Kretschmer (1934), Stockings (1940), and Mayer-Gross (1951) in various attempts to specify the analogy of the mescaline-induced state to schizophrenia.

Rinkel and colleagues began human experimentation with LSD in the United States in 1949. After a series of studies, they concluded that LSD was “an excellent tool for the investigation of experimentally produced psychotic-like manifestations” (Rinkel et al. 1955, p. 893). They also stated:

One cannot escape the impression, from these observations, that the socio-psychological behavior changes showed similarities with the general behavior of the mentally ill and that they provide fundamental implications in the field of psychotherapy. [p. 883]

The numerous studies alluded to above helped form the thesis that the chemically induced psychosis resulting from the administration of hallucinogenic agents was similar, if not altogether identical, to the “naturally” occurring functional psychoses, particularly schizophrenia. Not unexpectedly, what followed this wave of investigation was its logical antithesis—that is, that the drug-induced and schizophrenic states were markedly different, and could, in fact, easily be distinguished by professional observers (MacDonald and Galvin 1956; Hollister 1962; Jacobsen 1963). Where Rinkel et al. (1952) had described similarities in “disturbances of thought and speech; changes in affect and mood; perception; production of hallucinations and delusions; depersonalization and changes in behavior” (p. 577), Hollister (1968) cited differences in the type of hallucination (mainly visual for drug-induced states, mainly auditory in schizophrenia); frequency of delusions (common among schizophrenics, rare in drug-induced states); interpersonal relations (schizophrenics are characteristically withdrawn, while subjects with drug-induced psychoses prefer to have a companion); and speech (drug users’ speech is “usually related to reality” while schizophrenic speech is “vague, ambiguous and difficult to follow”) (p. 118).

Since the two Hollister studies are by far the most frequently cited ones in dispute of the hallucinogenic drug model of psychosis, they bear closer scrutiny.

Hollister’s (1968) findings coincide with those of others (Feinberg 1962; Malitz, Wilkens, and Essecover 1962; West 1975) in citing a predominantly visual hallucinatory pattern in drug subjects, as opposed to a primarily auditory pattern among schizophrenics. However, these observations were based on comparisons using chronic schizophrenic patients. Chapman (1966) interviewed 40 young schizophrenics (mean age = 24.6 years) with a recent onset of illness (average = 11 months’ duration) and discovered that disturbances in visual perception, including hallucinations, occurred with far greater frequency than disturbances in auditory perception. Young (1974) compared 20 recent onset schizophrenics (mean age = 19.5 years) with 20 age-, sex-, and occupation-matched LSD subjects and 9/20 schizophrenics. Young concluded that the two states are initially similar with regard to visual perceptual changes. A carefully controlled study by Freedman and Chapman (1973) found more changes in categories of visual perception than in auditory perception among “early” schizophrenics. McCabe et al. (1972) found that visual hallucinations occurred significantly more often in the acute than in the chronic schizophrenic state. Fischer (1972, p. 82) wrote:

...the perceptual and especially visual experiences of the incipient stages of schizophrenia are not unlike those induced by LSD or mescaline and auditory hallucinations only become prevalent after the process has lasted for some weeks or months.

Hoffer and Osmond (1960) suggested that visual perceptual disturbances occur with greater frequency in chronic schizophrenia than is generally reported, and that a gradual adaptation to these takes place over time. Similar explanations have been of-
ferred by Landis (1964) and Winters (1975).

The contention that auditory hallucinations are more characteristic of the schizophrenic than of the hallucinogenic drug state fails to acknowledge the importance of social and cultural factors (Al-Issa 1977). International studies of psychiatric populations have shown consistently that visual hallucinations are more common than auditory hallucinations among schizophrenics in the Near East and in Africa (Murphy et al. 1963; Jablensky and Sartorius 1975; Zarroug 1975). Cross-temporal studies of hallucinations in Western patients suggest that only recently has the frequency of auditory hallucinations exceeded that of visual hallucinations (Opler 1956; Al-Issa 1977). It is more prudent to assume that sociocultural and methodological differences account for the wide variations in data than to assume that the biological mechanism of schizophrenia differs from year to year, or from country to country. For the same reason, it is precipitous to label the LSD state a poor model of schizophrenia.

It is, in our view, quite mistakenly supposed that visual changes are the predominant perceptual anomalies in the LSD-25 experience, and that such happenings are rare in schizophrenia. We consider that neither of these propositions is true. Nevertheless, they have been used to suggest that the LSD-25 state is a poor model of schizophrenia.

Finally, in the only age-, sex-, and occupation-matched controlled study, 30 percent of LSD subjects and only 5 percent of schizophrenics reported auditory hallucinations (Young 1974). The data can be summarized with a minimum of contradiction by stating that the relative frequency of visual and auditory perceptual changes seen in chronic schizophrenia in the United States today may differ from that seen in hallucinogenic drug states, but that the frequency of such changes in acute or incipient schizophrenia closely parallels that which is seen in the drug states. Moreover, subjective reports on the nature of these perceptual changes suggest further areas of convergence (Horowitz 1964; Bowers and Freedman 1966; Grinspoon and Bakalar 1979). This is demonstrated in the following first-person accounts (S = schizophrenic; D = drug subject):

My senses seemed alive, they hit me harder. Things appeared clearer, I noticed things I had never noticed before. [Bowers 1968, p. 350] (S)

My senses became extremely acute. I could see an ant upon a tree at a great distance away. I could hear the whispering of my companion . . . far off from me. [Masters and Houston 1966, p. 153] (D)

I have noticed that noises all seem to be louder to me than they were before. It’s as if someone had turned up the volume. . . . I noticed it with most background noises. [McGhie and Chapman 1961, p. 105] (S)

Sensations were acute. I heard, saw, felt, smelled, and tasted more fully than ever before. . . . [Masters and Houston 1966, p. 10] (D)

Colors seem to be brighter now, almost as if they are luminous. When I look around me it’s like a luminous painting. [McGhie and Chapman 1961, p. 105] (S)

This “experience of heightened awareness” (Bowers 1968, p. 350) is common to hallucinogenic drug states and to acute psychosis. Phenomenological accounts supplement the quantitative data mentioned earlier, and support an analogy between the two states.

Phenomenological accounts of primary delusional experience reveal further similarities between the two states (Snyder 1974):

a sense of special significance began to invest everything in the room; objects which I would normally accept as just being there began to assume some strange importance. [Osmond 1970, p. 24] (D)

I became interested in a wide assortment of people, events, places and ideas which normally would make no impression on me. Not knowing that I was ill, I made no attempt to understand what was happening, but felt that there was some overwhelming significance in all this. . . . [MacDonald 1960, p. 218] (S)

This awareness of “significance”—the experience of expanded relevance or meaning—is the initial stage in the development of delusional thinking (Jaspers 1923; Lopez-Ibor 1974). The primary delusional experience is fundamental to hallucinogenic drug states and to incipient psychosis, and clearly precedes the development of systematized delusions (Bowers and
Freedman 1966; Bowers 1968). The greater frequency of systematized delusions in chronic schizophrenia (Hollister 1968) is merely a function of the duration of this altered experience. Interestingly, systematized delusions are quite frequent among chronic LSD users (Fisher 1968).

Withdrawal, as with systematized delusions, is a criterion which distinguishes between acute and chronic psychosis, but not between hallucinogenic drug states and acute endogenous psychosis. Many investigators have stated that schizophrenic withdrawal is a reflexive process in which the schizophrenic and those around him react to those aspects of the schizophrenic experience which are generally regarded as primary (Sadler 1953; Chapman 1966; Osmond 1969; Grinspoon and Bakalar 1979). Several studies have found similar withdrawal patterns associated with chronic LSD abuse (Fisher 1968; Glass and Bowers 1970; Davison 1975). Silverman (1969) states that withdrawal is characteristic of both hallucinogenic drug states and schizophrenia, and occurs in response to earlier perceptual changes of the type discussed above.

When LSD is ingested unwittingly, schizophrenic-like withdrawal is more likely to ensue. The following is a C.I.A. agent’s report on the effects of LSD administration to an unaware colleague. The “subject” was eventually found crouched beneath a highway overpass:

He reported afterwards that every automobile that came by was a terrible monster with fantastic eyes, out to get him personally. Each time a car passed, he would huddle down against the parapet terribly frightened. It was a real horror trip for him. I mean, it was hours of agony. It was like a dream that never stops—with someone chasing you. . . . It was awfully hard to persuade him that his friends were his friends at that point. He was alone in the world, and everyone was hostile. He’d become a full-blown paranoid. [Marks 1979, p. 71]

This description of a terrified, withdrawn individual is typical of the reaction to unaware ingestion of LSD (Lipton 1969; Marks 1979). In such cases, the tremendous bias introduced by the voluntary administration of a drug is eliminated. Such examples afford a more natural comparison with acute endogenous psychosis; they call attention to the advisability of distinguishing the two states on the basis that chronic schizophrenics are more withdrawn than voluntary drug subjects (Hollister 1968).

Another reported difference between hallucinogenic drug subjects and schizophrenics is in the area of speech production. To quote Hollister (1962, p. 82):

Both drug subjects and schizophrenics have difficulty expressing thoughts. In the former it may take the form of drunken ramblings, or when severe, incoherence, but what comes out is usually related to reality. Schizophrenic speech is often vague, ambiguous and difficult to follow. Weird symbolic representations abound, words may be confused with the objects they represent, and severe telescoping may result in the word salad. Drug subjects are usually greatly concerned about their failure to communicate; schizophrenics are not.

It is proposed here that the characteristics ascribed to schizophrenic speech pertain equally to drug subjects’ speech, and vice-versa. Six out of seven psychiatry textbooks (Bleuler 1924, p. 376; Henry 1938; Henderson and Gillespie 1940, p. 212; Sadler 1953, p. 407; Noyes and Kolb 1958, p. 396; Freedman, Kaplan, and Sadock 1976, p. 441; Day and Semrad 1978, p. 212) pulled randomly from the shelves of a medical school library use the word “incoherent” in reference to schizophrenic speech. Referring to the language of drug subjects, Grinspoon and Bakalar (1979) write, “words become confused with the qualities of the objects they designate” (p. 105) and “objects become charged with symbolic meanings” (p. 105). Krippner (1970) notes that hallucinogens may cause one to “effect a union between the word and its object” (p. 237). Snyder (1974, p. 60) reports that chronic LSD users are “out of touch with reality” and show “vague” thought patterns, which would imply a close resemblance to chronic schizophrenia according to Hollister’s schema. Likewise, one could label the speech of LSD subjects “vague, ambiguous and difficult to follow,” as an exchange between two LSD subjects demonstrates:

The interchange consumed one-half to three quarters of an hour, and went approximately as follows:

S-7: “And the way?”
S-8: “We try.”
S-7: “Holy waters.”
S-8: Makes some strange apparent sign of benediction over his own head and then makes the same sign toward S-7.

The contention that drug subjects, unlike schizophrenics, are “greatly concerned about their failure to communicate” pertains only to chronic schizophrenics. Chapman’s (1966)
study of recent onset schizophrenics showed them to be extremely concerned about their inability to communicate. One may appreciate that any psychological or physical loss breeds more concern during the period immediately following the loss than during a period several years after it is first experienced.

Another frequently cited “difference” between the schizophrenic and hallucinogenic drug states is that schizophrenics exhibit primarily dysphoric, anxiety-related affects, whereas drug subjects usually display euphoria (Young 1974). However, close phenomenological investigation reveals that the earliest affective changes in schizophrenia are often pleasurable and exhilarating (Chapman 1966; Bowers 1968; Osmond 1969; Docherty et al. 1978). Linton and Langs (1962, 1964) used “empirical scale” questionnaires to analyze the affective changes in LSD subjects. They found that most subjects initially experienced elation, but that this was followed by anxiousness and dysphoria as subjects felt that they were losing control over their thoughts. This progression of affective states parallels that which is observed in incipient schizophrenia.

Each of the reported differences between hallucinogenic drug states and endogenous psychosis examined above has been found to reflect a similarity between the two states. Mogar (1970) observed that no single feature or combination of features has been found to differentiate the two states. Hollister (1962, 1968) rightly argued that one should consider each state as a whole in order to make meaningful comparisons. Hollister’s (1962) study, in which tape recordings of schizophrenics and drug subjects were played before “blind” health professionals who were asked to distinguish them, is considered by many as proof that the two states have little resemblance. The study was beset by a number of problems, however. Foremost is the fact that chronic schizophrenics were used; for the reasons cited above, such a comparison is of limited value. In designing the study, Hollister cited “the differences in many particulars” (p. 80) between the states, and edited the tapes to include sections “illustrating some characteristic aspects of either schizophrenia or the three drug states” (p. 85). Thus the tapes were arbitrarily selected and edited to demonstrate characteristics that the author felt were distinctive of either one state or the other, but not common to both states. This introduces a tremendous degree of investigator bias. There were further problems, as the investigator stated:

Promptly it became apparent that the technique did not allow for complete blindness: drug subjects talked mainly in the present tense, schizophrenics in the past; drug subjects betrayed by accent and diction a generally higher level of education and social function than schizophrenics. For these reasons, specific instructions were given the raters to rate the interviews only on content, even if they had reason to believe the rating was actually in error. [Hollister 1962. pp. 85–86]

As Denber (1962, p. 91) comments in his discussion of this study, “[Hollister’s] statement reminded me of the judge telling the jury, after the prosecutor had made a telling point, to strike that mark from the record. Obviously it is impossible, once the raters know something about it, to say that we shall disregard those things.” Furthermore, some authorities believe that the drug doses that were used may have been too low (Grinspoon and Bakalar 1979). Despite these difficulties, authors who discount the hallucinogenic drug model of psychosis most often cite this study (and Hollister 1968) as convincing evidence of the model’s shortcomings. In contrast, Hoffer (1956) taped verbatim interviews with an LSD subject and an acute schizophrenic. The recordings were then played before a group of experienced psychiatrists who were unable to distinguish the patient from the drug subject. Ironically, many years after his original studies, Hollister reevaluated his position. In comparing new onset schizophrenia to the LSD state, he acknowledged “a greater resemblance than was formerly thought” (Hollister 1978, p. 416).

It would seem, then, that the case against the hallucinogenic drug model of psychosis has several weaknesses. The argument for an analogy between the two states must demonstrate that they share certain fundamental properties. In the following pages, consideration is given to these fundamental properties, and the analogy is expanded to include dream states.

Ego Boundaries

Savage (1955) traced all of the phenomena experienced within the LSD state to a primary loss or decathexis of the ego boundaries, a concept derived from Federn (1952). Freeman, Cameron, and McGhie (1958) considered the decathexis of the ego boundaries to be the fundamental disturbance from which all other manifestations of schizophrenia followed. Fliess (1973) viewed the decathexis of the ego boundaries as the necessary condition for hallucinatory wish fulfillment in dreams.

To understand what is meant by the term “ego boundaries,” one must
review Federn's original concept and the subsequent revision and interpretation it has undergone in the literature. Federn used the term to denote a dynamic set of temporospatial limits which divide experience into past, present, and future; internal and external; real and unreal. For Federn, the ego presented a unique paradox because it is normally experienced as both subject and object at once. Jacobson (1954, p. 520), using Hartmann's (1950) distinction between "ego" and "self," noted that Federn's subject and object components of the ego corresponded to the "system ego" and the "self-representation," respectively. Federn's "ego boundary" is identical with the boundary between self-representation and object-representation (Jacobson 1954).

From clinical observation, Federn noted that in incipient psychosis or, in healthy persons, upon falling asleep, the ego (self-representation) boundaries lose their cathectic. Enlarging upon Federn's observations, Spiegel (1959) wrote that the accurate perception of reality depends upon the ego's continuous averaging of self-representations to form a constant frame of reference: the self. The regressive loss of this averaged self-representation in dreams and psychosis leads to a chaotic condition in which various ego states succeed one another without a common reference point. This renders a loss of temporal continuity to experience. The hypnagogic phenomena described by Isakower (1938) are prototypical of such experience. Moreover, internal processes can no longer be distinguished from external ones. Sensory phenomena strike the weakened ego boundaries with unaccustomed impact; colors and sounds are imagined as having increased intensity. The distinction between self and nonself is blurred. In this state of altered temporal and spatial relationships, the notion of causality is secondarily affected. Thelmar (1937, p. 253) stated, commenting on her own psychosis, "lunatics do not 'lose their reason': they merely reason from false premises."

While Federn's observations of this phenomenon were confined to schizophrenic and dream states, others have described a similar process in hallucinogenic drug states (Linton and Langs 1962; Cohen 1964; Barr et al. 1972). Sarlin (1962) considered the withdrawal of cathectic from the self-representation to be the basis for depersonalized states in general. The following accounts typify the kind of primary experience which such formulations attempt to reconstruct:

I became aware of the body that encased me as being very heavy and amorphous. Inside it, everything was stirring and seemed to be drawing me inward. [Masters and Houston 1966, pp. 9-10] (D)

I feel as though I'm not alive—as though my body is an empty, lifeless shell. I seem to be standing apart from the rest of the world. [Bockner 1949, p. 969] (S)

The decathexis of the self-representation in dreams, hallucinogenic drug states, and acute psychosis results in a dichotomous experience characterized by a weakening of the ego's identification with the self. The ego, the structure to which we attribute the function of perception, including perception of the self (Hartmann 1950), only partially and imperfectly perceives a relation to the self. Writers have used a variety of terms to describe this dichotomy. Kleinman, Gillin, and Wyatt (1977, p. 573) describe LSD subjects and schizophrenics who experience a "separation of body and soul." One of Klee's (1963, p. 463) LSD subjects states, "I feel like I'm a bystander watching myself." Jacobson (1959, p. 608) wrote that the depersonalized state which often heralds an acute schizophrenic psychosis results from a "schism" in the ego. Linton and Langs (1964, p. 480) reported for their LSD subjects that "the observing self became dissociated from the experiencing self." Stamm (1962) and Arlow (1966) observed that this dissociation comprised the basis of depersonalized states; the latter author emphasized its occurrence in dreams. Laing (1965, p. 71) mentioned "a divorce of self from body" in describing the schizophrenic existence.

What links these various characterizations is that each describes an estrangement of the "participating" self from the "observing" or perceiving agent. This estrangement is the essential or enabling mechanism in the everyday occurrence of daydreams and transient depersonalizations. It consists initially in a disruption of the ego's ongoing synthesis of the various self-representations into a continuous, coherent self. A sustained disruption compromises the ego's perception of the relationships between individual self-representations. Eventually, the connections may be lost; the ego may identify with one or another self-representation, but can no longer identify with a continuous, coherent self. It is to this process that Federn loosely refers in describing a decathexis of the ego boundaries. This estrangement is the fundamental process which is seen alike in dreams, hallucinogenic drug states, and acute psychosis. Its relation to the loss of reality testing and the emergence of the primary process in these three states can now be made clear.

Freud (1917, p. 231) noted "the great practical importance of dis-
distinguishing perceptions from ideas, however intensely recalled. Our whole relation to the external world, to reality, depends on our ability to do so.” Rapaport (1951) recognized that the discrimination between idea and perception depends upon one’s capacity for “reflective awareness,” which he defined as follows:

It seems to be a sub-species of the function that distinguishes imagery from hallucination and percept, thought from reality. The following are some form-variables of reflective awareness: ideation without specific awareness, ideation with awareness, awareness with awareness that one is aware, etc. (p. 302)

Schafer (1968, p. 91) enlarged upon this reasoning. He stated that reality testing requires an ability to represent “oneself as thinker of the thought—what shall henceforth be called the reflective self representation” (author’s italics). Schafer argued that the suspension of reflective self-representation enables the turning away from reality in dreams and psychosis. Moreover, he surmised that this is what Freud (1938, p. 276) alluded to in describing the “splitting of the ego” which occurs in these states. Thus Schafer relates the loss of reality in dreams and psychosis to the dichotomous experience described above. Reflective awareness, or reflective self-representation, requires complete identification between the perceiving agent (“thinker of the thought”) and the participating self. In dreams, hallucinogenic drug states, and psychosis the participating self is represented as a series of discontinuous selves or parts of selves. Reflective self-representation is suspended; reality is lost. Without the coherent organization of various self-representations into a continuous self, the secondary process is impaired, and the primary process predominates.

Noy (1969) observed that the secondary process depends upon: (1) the capacity to maintain a constant inner representation of the self and of objects; (2) the capacity to distinguish between self and object and thus between internal and external phenomena; (3) the capacity to shift from “thing-presentation” to “word-presentation.” We have seen that the ability to meet the first two criteria is impaired in the three states under consideration. We may now call attention to the third criterion.

Freud (1917) elaborated on the mechanism by which primary process transformations occur in dreams:

In this process thoughts are transformed into images, mainly of a visual sort; that is to say, word-presentations are taken back to the thing-presentations which correspond to them. . . . The primary psychical process is brought to bear on these memories, till, by condensation of them and displacement between their respective cathexes, it has shaped the manifest dream content. (p. 228)

Arieti (1955, p. 244) has observed this process, which he calls “perceptualization of the concept,” in the evolution of schizophrenic hallucination. Klee (1963, p. 467) noted the “visual, hallucinatory quality” of the thought of LSD subjects. Both Arieti, in describing schizophrenics, and Klee, in describing LSD subjects, relate this regressive transformation to the “concrete attitude” described by Goldstein (1944). Goldstein defined the concrete attitude as one in which the subject is unable to transcend the immediate sensory impressions imparted by the environment and proceed to the level of conceptual thinking and abstraction. From similar observations, Salzinger (1971) developed an “immediacy hypothesis” which seeks to explain schizophrenic symptomatology by this phenomenon. Hartocollis (1980, p. 862) wrote, “In a dream everything is experienced much more immediately than in awakeful reality.” Concerning LSD subjects, Klee (1963, p. 469) wrote, “The relationship to objects, including people, takes on an unusual quality and depth and an immediacy which dissolves the ordinary experience of continuity from moment to moment.” It is this quality of vivid, immediate sense-imagery which characterizes the primary process. Its presence signifies an impairment of the secondary process and a regressive transformation from a word-presentation to a thing-presentation mode of thought.

Freud (1900, p. 295; 1915, p. 199) observed that in dreams and in schizophrenia words undergo condensation and displacement via the primary process; this produces the neologisms and other transformations which characterize schizophrenic speech. The same transformations have been observed in LSD states (Savage and Cholden 1956; Klee 1963; Grinspoon and Bakalar 1979). Flies (1953) observed that the dreamer treats verbal residues in the manner of a schizophrenic—words are not conceived as symbols of objects, but as objects themselves. Identical observations have been made regarding the hallucinogenic drug state (Krippner 1970; Grinspoon and Bakalar 1979) and schizophrenia (Hollister 1968). Fisher (1954) concluded from his tachistoscope experiments that in dreams visual percepts are treated concretely as objects, and as such, are subjected to the transformations of the primary process in much the same way that Freud described for verbal residues. The theme echoed by all of these writers is that in all three
states the net effect of these transformations is a tendency toward concretization. Rivers (1923) and Silberer (1909) have observed this tendency in dreams and hypnogogic states, respectively. McGhie and Chapman (1961) and Weckowicz, Somner, and Hall (1958) documented the same tendency in schizophrenics. DeShon, Rinkel, and Solomon (1952) and Silverstein and Klee (1958) noted deficits in abstract thinking on proverb tests given to LSD subjects.

McKellar (1957, 1963) explained the loss of abstract thinking in schizophrenia, dreams, and mescaline states as the result of an inability “to inhibit associated but irrelevant ideas” (1957, p. 104). Conversely, Arieti (1955) saw the concrete attitude as the basis for the associationistic disturbance in schizophrenia. Many writers in the schizophrenia literature have emphasized the associational or attentional disorder in their respective theories of the disease (Bleuler 1911; Cameron 1944; McGhie and Chapman 1961). Venables (1964) employed the term “input dysfunction” in an attempt to unify these related concepts of schizophrenia.

Much research in the last two decades has been devoted to the study of psychophysiological paradigms of this input dysfunction. Claridge (1978) found a strong similarity between acute schizophrenics and LSD subjects on measures of electrodermal sensitivity and twoflash thresholds. Silverman (1968, 1969) reviewed the literature on various laboratory measures of sensory responsiveness in LSD subjects and schizophrenics. He related the results of these psychophysiological studies to reports of the subjective experience of these states, which suggest that a heightening of sensory awareness takes place:

These studies are consistent with the subjective report literature; they indicate that during a schizophrenic reaction and under the influence of psychedelic drugs, (1) ordinary-intensity stimuli are experienced more intensely than normally; and (2) less sensory information is necessary in order to report that a stimulus is present. [Silverman 1969, p. 198]

A one-time schizophrenic patient described her first-hand experience of the “input dysfunction”:

The mind must have a filter which functions without our conscious thought, sorting stimuli and allowing only those which are relevant to the situation in hand to disturb consciousness. . . . What had happened to me . . . was a breakdown in the filter and a hodge-podge of unrelated stimuli were distracting me from the things which should have had my undivided attention. . . . By the time I was admitted to the hospital I had reached a stage of "wakefulness" when the brilliance of light on a window sill or the color of blue in the sky would be so important it could make me cry. I had very little ability to sort the relevant from the irrelevant. The filter had broken down. Completely unrelated events became intimately connected in my mind. [MacDonald 1960, pp. 218-219]

The passage simultaneously illustrates the interrelatedness of the input dysfunction, heightened sensory awareness, and the primary delusional experience in schizophrenia.

Terms like “input dysfunction,” “immediacy hypothesis,” and “concrete attitude” designate qualities that reflect the operation of the primary process. Earlier it was argued that the impairment of the reality-oriented secondary process is related to a disruption in the ego’s normally continuous and implicit identification with the self. The impairment of the secondary process enables the emergence of the florid characteristics of the primary process. Thus, many of the well-described traits of dreams, hallucinogenic drug states, and acute schizophrenia can be related to what has been called a decathexis of the self-boundaries, or more specifically, to a disruption of the ego’s ongoing synthesis of self-representations into a continuous, coherent self. This relationship can be partly explained by, and readily seen, in discussing the altered experience of time that occurs in the three states (MacKenzie 1965).

Speaking of dreams and psychosis, Freud (1900, p. 91) wrote, “In both there is a complete lack of sense of time.” Review of the literature on the sense of time in schizophrenia and hallucinogenic drug states reveals consistent subjective reports of “timelessness,” time “standing still,” or time “slowed down” (Schilder 1936; Scott 1948; Savage 1955; Klee 1963; Hartocollis 1975; Grinspoon and Bakalar 1979). Hartocollis (1980, p. 863) wrote, “The dreamer’s temporal orientation is strictly in the present . . .” Arieti (1955, p. 240) wrote of the schizophrenic, “The temporal orientation of the patient becomes gradually limited to the present time.” Anderson and Rawnsley (1954, p. 47) found that LSD produced “a sense of temporal insularity in which only the present was real, past and future being exceedingly remote.” As Arieti (1955) points out, all thinking occurs in the present tense. When one thinks about the past or the future, the actual thoughts take place in the here-and-now. To differentiate memories and expectations from present events, one must appreciate the relationship between the self-representation associated with the memory or expectation, and the self-representation associated with the present thought. If this relationship is not appreciated,
the distinction between past, present, and future dissolves. In dreams, hallucinogenic drug states, and psychosis, the normal continuity of experience is disrupted. The ego perceives a number of disparate self-representations in lieu of a continuous self. At first the relationship among these self-representations is uncertain. Eventually, no meaningful relationship is perceived. Ordered existence is replaced by a sense of timelessness; past, present, and future are as one.

I don't feel things are ordered. I have lost the sequence of events. [Rosser 1979, p. 183] (S)

I was not experiencing events in the normal sequence of time. I was experiencing the events of 3.30 [P.M.] before the events of 3.0; the events of 2.0 after the events of 2.45, and so on. [Mayhew 1956, pp. 294–295] (D)

**Biological Considerations**

It will be noted that the quotations given in the introduction to this article emphasized the connection between dreams and endogenous psychosis. The subsequent section was principally concerned with the analogy between endogenous and drug-induced psychosis, though the analogy was extended to dreams where appropriate. The final section emphasizes the biochemical, anatomical, and neurophysiological correlates of the analogy between dreams and hallucinogenic drug states.

Aserinsky and Kleitman (1953) discovered the existence of a regular periodicity within sleep. Because of the regular occurrence of episodes which featured rapid eye movements at approximately 90-minute intervals, the term REM sleep was coined. When subjects were awakened during REM sleep, dream recall occurred with much greater frequency than when subjects were awakened at other times, termed non-REM (NREM) sleep. These results were reproduced by several investigators (Dement and Kleitman 1957; Goodenough et al. 1965; Stoyva and Kamiya 1968; Feinberg 1970; Snyder 1971). The studies showed that dreams which occurred during REM sleep were characterized as being vivid, intense, affectively charged, and filled with bizarre imagery of a predominantly visual nature. Dreams were occasionally recalled from NREM sleep awakenings. These were described as "being more contemporary and more thought-like in character than the narratives elicited from REM sleep" (Feinberg 1970, p. 126). Based on the preceding discussion, it seems that REM sleep dreams reflect the active primary process and a regression to the perceptual mode of psychic function, whereas the dreams of NREM sleep display characteristics intermediate to those of REM sleep and waking life; they reflect an impaired secondary process without the florid attributes of the pure primary process.

Intensive investigation into the physiological correlates of REM and NREM sleep led to the monoamine theory of sleep states introduced by Jouvet (1960, 1972, 1974). Briefly stated, this theory implicated the serotonergic neurons of the raphe system—extending rostrally in the midline from the caudal medulla to the caudal mesencephalon (Anden et al. 1965, 1966a; Dahlstrom and Fuxe 1964, 1965; Fuxe 1965)—in the mechanisms of NREM sleep as well as in the "priming" of REM sleep (Jouvet 1972). It was postulated that noradrenergic fibers of the locus ceruleus, a structure located in the lateral part of the brainstem tegmentum (Dahlstrom et al. 1964; Anden et al. 1966a, 1966b), were responsible for the "executive mechanisms" of REM sleep (Jouvet, 1972). The theory was based on lesion experiments and neuropharmacological manipulations in the cat. The advent of intraneuronal micro-electrode recording techniques brought about a substantial revision of this theory. It has become possible to monitor the firing rates of neurons of the raphe system (particularly those within the dorsal raphe nucleus, the most rostral member of the raphe system) as well as other brain sites, including the locus ceruleus. By this technique, one can estimate the activity of these neuronal groups throughout waking and sleeping states. Such studies have shown that unit activity of cat dorsal raphe neurons undergoes a substantial reduction as the animal enters NREM sleep from the waking state (McGinty and Harper 1976; Trulson and Jacobs 1979d). A further reduction in firing rate occurs when the animal goes from NREM to REM sleep. Thus there is a progressive diminution of serotonergic outflow from the dorsal raphe nucleus as the animal progresses from the waking state through NREM sleep into REM sleep. During REM sleep these serotonergic neurons are virtually silent (Trulson and Jacobs 1979b; Sakai and Jouvet 1980). A similar, but less pronounced pattern of unit activity has been observed for the norepinephrine-containing neurons of the locus ceruleus (Hobson, McCarley, and Wyzinski 1975).

These observations correlate well with pharmacological findings. Numerous drugs cause decreases in the ratio of REM sleep to total sleep time, but very few can effect an increase in this ratio (Jacobs 1978). Reserpine depletes intraneuronal stores of serotonin as well as catechola-
Several studies have shown that reserpine causes an increase in REM sleep time in man (Tissot 1965; Hartmann 1966; Hoffman and Domino 1969; Coulter, Lester, and Williams 1971) and in other animals (Khaban and Sawyer 1964; Reite et al. 1969; Stern and Morgane 1973). This is precisely what one would predict based upon the findings of the intracellular recording studies; reduced neurotransmitter content within monoaminergic neurons is the hypothesized behavioral equivalent of diminished firing rates. Conversely, an increase in available neurotransmitter should be the behavioral equivalent of an increased firing rate. Monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants are thought to act by increasing the synaptic availability of serotonin and catecholamines. It has been shown that MAOIs consistently suppress REM sleep time in man (Wyatt et al. 1971a, 1971b; Wyatt 1972). MAOIs may have a more pronounced effect on serotonin than on norepinephrine levels (Pscheidt 1964; Sourkes 1972). In the cat, MAOIs selectively increase brain serotonin levels without exerting significant effects on other neurotransmitter systems (Pscheidt, Morpurgo, and Hinchwich 1964). A complete abolition of REM sleep occurs when MAOIs are administered to cats (Jouvet 1967). These studies suggest that the REM sleep suppressing effect of MAOIs is primarily due to their effect upon serotonergic neurotransmission.

The results obtained with tricyclic antidepressants support the notion that REM sleep depends on the activation state of serotonin-containing neurons. Dunleavy et al. (1972) administered six different compounds within this pharmacological class to normal volunteers over a 4-week period. Each drug suppressed REM sleep time to varying degrees. Particularly germane to the present hypothesis is that chlorimipramine, which is a strong serotonin reuptake blocker but only a weak norepinephrine reuptake blocker (Carlsson et al. 1969a, 1969b), was found to be the most potent inhibitor of REM sleep (Dunleavy et al. 1972). This finding has recently been duplicated (Leckman et al. 1980). Chlorimipramine is also the only tricyclic antidepressant that has been shown to produce profound REM sleep suppression in depressed patients (Pasquali et al. 1971). The ability of chlorimipramine to suppress REM sleep is thought to constitute the basis for its effectiveness in the pharmacological treatment of narcolepsy (Mendelson, Gillin, and Wyatt 1977; Chen 1980). Narcolepsy is considered to be a disorder of the mechanism that controls REM sleep (Rechtschaffen and Dement 1969). The frequent occurrence of hypnagogic (and hypnopompic) hallucinations is a prominent symptom of this disorder. Shapiro (1975) found that chlorimipramine therapy can alleviate these symptoms in narcoleptic patients within 48 hours. It is interesting to consider these findings in the light of Federn’s (1952) observations on hypnagogic hallucinations. It will be recalled that Federn attributed this phenomenon to a withdrawal of cathexis from the ego boundaries. Drugs which prevent the occurrence of hypnagogic hallucinations must (if one accepts Federn’s observation) somehow be able to counteract this withdrawal. In this respect, one notes that chlorimipramine was found to be more effective than imipramine in the treatment of narcolepsy, presumably because of the chlorimipramine’s greater relative potency at serotonergic synapses (Guilleminault, Carskadon, and Dement 1974). This finding fits nicely with the aforementioned work with MAOIs in man and in the cat in implicating serotonergic systems in the regulation of REM sleep. To return again to Federn’s conceptualization, it is as though the neurochemical analogue of the ego boundary cathexis is serotonergic outflow. When this outflow is diminished, as in REM sleep, a withdrawal of ego boundary cathexis also occurs. When this outflow is bolstered by the administration of tricyclic antidepressants or MAOIs, the hypnagogic hallucinations of narcolepsy are eliminated and REM sleep is suppressed. While this obviously simplistic analogy conforms well with the original Freudian model of neuronal cathexis (Freud 1895), it is offered here merely to suggest an intriguing parallel. As will be seen however, this parallel fits nicely with other findings, and may have implications in the treatment of schizophrenia which, as noted earlier, is believed by some investigators to result from a withdrawal of ego boundary cathexis (Freeman, Cameron, and McGhie 1958).

Wooley and Shaw (1954), noting the structural similarity of the LSD and serotonin molecules, postulated that a blockade of central serotonin receptors might account for LSD’s psychotomimetic effects. They proposed, in effect, a serotonin hypothesis of schizophrenia, which held that interference with normal serotonergic neurotransmission might result in a schizophrenic psychosis. This hypothesis eventually fell into disfavor for reasons to be considered below. It did, however, succeed in prompting an investigation into the effects of LSD on brain serotonin metabolism. Rosecrans, Lovell, and Freedman (1967) found that LSD caused a decrease in rat brain
serotonin turnover. Aghajanian, Foote, and Sheard (1968) used an intraneuronal recording technique to demonstrate that intravenous or intraperitoneal administration of LSD to rats resulted in a sharply reduced firing rate in neurons of the midbrain raphe nuclei, but not in neurons outside of the midbrain raphe. These raphe neurons were identical with the serotonin-containing neurons described by Dahlstrom and Fuxe (1964, 1965). Further experiments revealed that this reduction in unit activity was due to a direct effect of LSD on the cell bodies of these neurons (Haigler and Aghajanian 1973). It was shown that 2-bromo-LSD, a congener of LSD without hallucinogenic properties, was much less effective than LSD in inhibiting unit activity of dorsal raphe neurons, and could not produce complete inhibition even when administered in extremely high doses (Aghajanian, Foote, and Sheard 1970). This result coincided with earlier findings that 2-bromo-LSD did not affect central serotonin metabolism even when given in significantly higher doses than those at which LSD decreased central serotonin turnover (Freedman 1961; Rosecrans, Lovell, and Freedman 1967). Since LSD and 2-bromo-LSD are equipotent in peripheral serotonergic systems, this raised the possibility that the unique inhibitory effect of LSD upon the discharge rate of dorsal raphe neurons might account for its hallucinogenic properties.

This latter possibility received support from the finding that LSD, psilocin, 2,5-dimethoxy-4-methylamphetamine (DOM), N, N-dimethyltryptamine (DMT), mesdcaline, and 5-methoxy-DMT, which have similar if not identical psychological effects and which show a high degree of cross-tolerance with each other (Jacobs and Trulson 1979a), all exert a marked inhibitory effect upon dorsal raphe neurons (Aghajanian, Foote, and Sheard 1970; Aghajanian and Haigler 1975; Mosko and Jacobs 1977; Jacobs 1978). Moreover, the relative potency of these hallucinogenic drugs in depressing the discharge rate of these neurons corresponds to their relative potency in various psychological and perceptual measures in man (Wolbach, Miner, and Isbell 1962; Snyder, Faillace, and Hollister 1967; Szara 1970; Trulson, Stark, and Jacobs 1977). Thus, every major member of the class of hallucinogenic drugs, agents which can cause an altered state of consciousness that shares several common properties with dreams and with acute schizophrenia as outlined above, is uniquely capable of exerting a pronounced inhibitory effect upon the soma of serotonin-containing neurons of the dorsal raphe nucleus. Other psychoactive drugs, such as the opiates, the belladonna alkaloids (atropine), and tetrahydrocannabinol (THC), do not exert this primary physiological action, and produce altered states of consciousness which are clearly distinguishable from those produced by hallucinogenic drugs (Jacobs 1978; Jacobs and Trulson 1979a).

Closely allied to the serotonin hypothesis of schizophrenia was the REM phasic event intrusion hypothesis (Dement et al. 1969). This hypothesis held that a defective serotonin gating mechanism allowed some phasic events of REM sleep to intrude into the waking state. It was based on the observation that pharmacological or ablative interference with serotonergic neurotransmission enabled the emergence of pontine-geniculate-occipital (PGO) waves, monophasic slow potentials which are normally confined to REM periods, into the NREM and waking states. The occurrence of these waves seemed to coincide with hallucinatory-like behaviors in animals. It was proposed that PGO waves were the "minimal neural substrate" (Dement et al. 1969, p. 792) of dream images, and that the intrusion of PGO waves into the waking state might give rise to the hallucinations of schizophrenia.

Further research demonstrated, however, that the eye movements of REM sleep occur just before PGO waves in the lateral geniculate body (Sakai and Cespuglio 1976). Therefore, the notion that eye movements occur in response to hallucinated visual images caused by the intrusion of phasic PGO waves must be rejected (Jouvet 1979). Furthermore, REM sleep occurs without interruption even after complete destruction of the ascending PGO system (Lauret et al. 1977; Jouvet 1979). Thus PGO waves are not the "minimal neural substrate" of dream images.

Just as it was theorized that PGO waves could explain the visual hallucinations of schizophrenia, so they were invoked to explain the LSD state. Since PGO waves were known to be under serotonergic control, and since LSD was known to inhibit the discharge of serotonin-containing neurons, it was reasoned that LSD might produce waking hallucinations by introducing PGO waves into the waking state (Stern, Morgane, and Bronzino 1972). Experiments showed that LSD in fact confined PGO waves to REM periods (Henriksen, Jacobs, and Dement 1979; Brooks 1975; Ruch-Monachon, Jaliffre, and Haefely 1976). Thus PGO waves are not the neural substrates of drug-induced hallucinations. Jouvet (1979) has concluded that PGO generators are responsible for the motoric programming of oneiric behavior.
Serotonin or Dopamine?

While enthusiasm for the intrusion hypothesis had given new impetus to the serotonin hypothesis of schizophrenia, its demise helped throw the latter into disfavor (Mendelson, Gillin, and Wyatt 1977). At the same time, the dopamine hypothesis gained ascendancy. This hypothesis is based upon two major findings: (1) Pharmacological agents that decrease dopaminergic activity have antipsychotic properties, and (2) amphetamine increases dopaminergic activity, and is considered by some investigators to produce a state that is virtually indistinguishable from paranoid schizophrenia (Meltzer and Stahl 1976). The dopamine hypothesis may be in jeopardy (Alpert and Friedhoff 1980). Amphetamines may enhance the therapeutic effect of phenothiazines (Fukuda and Mitsuda 1979) and reduce psychotic symptoms (Van Kammen et al. 1982) in schizophrenia. A review of the literature on the use of MAO inhibitors (which theoretically increase dopaminergic activity) in schizophrenia showed that these drugs either ameliorate or have no effect upon the core psychopathological symptoms of schizophrenia (Brenner and Shopsin 1980). When L-dopa was added to phenothiazine regimens in the treatment of several independent groups of schizophrenics, additional clinical improvement was observed (Fleming, Makar, and Hunter 1970; Inanaga et al. 1975; Meltzer and Stahl 1976). Alpert and Friedhoff (1980) suggested that the timing of the onset of amphetamine psychosis coincides more closely with dopamine depletion than increased availability. All of the above results would make a good case for dopaminergic hypoactivity, rather than hyperactivity, as being of etiological significance in schizophrenia.

While it is likely that dopamine plays some role in the pathogenesis of schizophrenia, it is apparent that there are a number of problems with the dopamine hypothesis. Its ascendancy has gone hand in hand with the ascendancy of the amphetamine model of psychosis. In regard to the latter, Claridge (1978) has argued recently that the LSD state is a better model psychosis than the amphetamine model. Recent work with animal models of psychosis may clarify this issue. In a series of experiments, Trulson, Jacobs, and colleagues developed a reliable model for assessing behavioral responses to a number of psychoactive drugs. They observed the full behavioral repertoire of cats in response to various drugs and noted in particular that limb flicks and abortive grooming were produced consistently by LSD, psilocin, psilocybin, DMT, DOM, and mesacline (i.e., all major hallucinogenic drugs) and by parachlorophenylalanine (PCPA), an inhibitor of serotonin synthesis (Trulson and Jacobs 1976; Jacobs, Trulson, and Stern 1976, 1977; Jacobs et al. 1977). These behaviors were not seen following the administration of a variety of other psychoactive drugs, including amphetamine (Jacobs and Trulson 1979b). In another experiment, the investigators administered 5-methoxy-DMT, a short-acting hallucinogen, and simultaneously measured both the discharge rate of dorsal raphe neurons (using subcortical micro-electrodes) as well as the number of instances of abortive grooming and limb flicks (Trulson and Jacobs 1979b). Both measures showed very clear dose-response relationships. Decreases in unit activity in the dorsal raphe were correlated with increased behavioral responses. This was cited as strong evidence in favor of the serotonin hypothesis of hallucinogenic drug action. The investigators also related their experiment to an earlier one in which dorsal raphe unit activity was recorded in freely moving cats (Trulson and Jacobs 1979d). That study demonstrated a dramatic decrease in the rate of dorsal raphe unit discharge as the animal went from waking to NREM sleep to REM sleep. Jacobs and Trulson (1979d) concluded:

The oft-noted phenomenological similarity of dreams (which occur most vividly in REM sleep) and drug-induced hallucinations might be mediated, in part, by a common neurochemical event—the inactivation of central serotonergic neurotransmission. [p. 401]

The Trulson and Jacobs model was based on their experiments which showed that only hallucinogenic drugs produced "hallucinatory-like" behaviors in cats (including limb flicks and abortive grooming), and that all drugs which produced these behaviors were known to depress serotonergic neurotransmission (Jacobs 1978). This model was challenged by a report that long-term amphetamine administration in the cat led to a number of hallucinatory behaviors, including limb flicks and abortive grooming (Ellinwood and Kilbey 1977). This report encouraged Trulson and Jacobs (1979c) to re-examine the effects of amphetamine administration upon behavior and serotonin metabolism in the cat. They found that short-term administration of amphetamine did not elicit the behaviors in question, and produced a small decrease in brain serotonin without any decrease in 5-hydroxyindoleacetic acid (5-HIAA), the primary metabolite of serotonin. However, long-term amphetamine administration on a dosage schedule equivalent (on a milligram of drug/kilogram of body weight basis)
to that which typically produces amphetamine psychosis in humans produced the "hallucinatory" behaviors and resulted in large decreases in serotonin and 5-HIAA in all brain regions examined. The appearance of the behaviors and the serotonin decrements followed a time-course that parallels the typical appearance of psychotic symptoms in human amphetamine psychosis.

Thus, the serotonin hypothesis can account for the onset of "hallucinatory" behaviors in both the amphetamine model and the hallucinogenic drug model of psychosis in the cat. An identical time course for the appearance of hallucinatory behaviors following chronic amphetamine administration has been seen in rats (Nielsen, Lee, and Ellison 1980) and in monkeys (Ellison, Nielsen, and Lyon 1981). Since the time course of these behaviors is virtually identical to that which is seen in humans, there is a strong possibility that changes in serotonergic neurotransmission may occur in the chemical model of psychosis in man.

The serotonergic model of dreams and hallucinogenesis presented above has a number of difficulties. In cats, the behavioral effects of LSD outlast the depression of dorsal raphe unit activity by several hours (Trulson and Jacobs 1979a). Readministration of LSD 24 hours after the initial dose produces marked depression of raphe activity, but little behavioral effect. Dissociations between raphe unit depression and "hallucinatory" behaviors have also been seen with other hallucinogens (Trulson, Heym, and Jacobs 1981). Lisuride, an ergoline derivative, exerts a rapid, direct inhibitory effect on dorsal raphe neurons (Rogawski and Aghajanian 1979), produces limb flicks and abortive grooming in cats (White, Hohean, and Appel 1980; Marini et al. 1981), but is not hallucinogenic in man. Mescaline, unlike other hallucinogens which produce a direct effect, produces only an indirect suppression of dorsal raphe unit activity (Haigler and Aghajanian 1973). As for the dramatic depression of raphe units that occurs during REM sleep, a recent experiment involving pontine-lesioned cats that display REM sleep without atonia suggests that the discharge rate of raphe units may reflect changes in motoric activity rather than changes in state of consciousness (Trulson, Jacobs, and Morrison 1981). The lesioned cats showed only a small decrease in raphe unit activity in passing from waking to NREM sleep to REM sleep compared with nonlesioned controls.

These findings question the significance of the discovery that dorsal raphe neurons behave similarly in REM sleep and in hallucinogenic drug states. Nevertheless, the preponderant evidence currently favors a role for a common mechanism, depressed serotonergic neurotransmission, in these states (Jacobs and Trulson 1981; White and Appel 1982).

Mandell (1980) tested a variety of psychoactive agents and found that only hallucinogens inhibit raphe cell firing without a compensatory increase in serotonin synthesis. When LSD is given in conjunction with PCPA, an inhibitor of serotonin synthesis, the effects are synergistic (Trulson and Jacobs 1976). In man, depletion of serotonin by reserpine enhances the effects of hallucinogens (Isbell and Logan 1957; Freedman 1963; Resnick, Krus, and Raskin 1965). MAOIs (which theoretically increase serotonergic neurotransmission) attenuate the effects of hallucinogens (Sai-Halasz 1963; Resnick, Krus, and Raskin 1964) and suppress REM sleep. LSD hastens the onset and prolongs the duration of REM periods (Muzio, Roffwarg, and Kaufman 1966).

Other data that suggest convergent mechanisms have implications for schizophrenia. LSD and PCPA produce identical "hallucinatory" behaviors in cats (Dement et al. 1969; Trulson and Jacobs 1976). PCPA-treated cats do not exhibit a REM rebound after experimental REM sleep deprivation. Human sleep studies have shown consistently that acute schizophrenics do not have a REM rebound after experimental REM sleep deprivation (Neale and Oltmanns 1980). In man, PCPA administration suppresses REM sleep, but is not followed by a REM rebound upon drug termination (Mendelson, Gillin, and Wyatt 1977). The REM sleep abnormality and hallucinatory behaviors produced by PCPA in cats are reversed by administration of 5-hydroxytryptophan, a serotonin precursor, or by chlorpromazine, a drug used in the treatment of schizophrenia (Zarcone 1979). There is a substantial body of electrophysiological (Miller et al. 1975; Dray et al. 1976; Bunney and Aghajanian 1976), anatomical (Miller et al. 1975; Pradhan and Bose 1978), behavioral (Costall and Naylor 1974; Costall et al. 1975; Giambalvo and Snodgrass 1978; Waldmeier and Delini-Stula 1979; Carter and Pycock 1979), and biochemical (Kuczenski 1979) evidence in support of a putative role for serotonin in the direct inhibition of dopaminergic neurotransmission in the substantia nigra, neostriatum, and nucleus accumbens. A depression of serotonergic neurotransmission, which, as detailed above, is precisely what takes place during hallucinogenic drug and REM sleep states, would result in a loss of this inhibitory influence. Such a mechanism
could be invoked to explain the putative dopaminergic hyperactivity within these structures which forms the basis of the dopamine hypothesis of schizophrenia.

It is well established that an understanding of interactions among neurotransmitters is a crucial step toward understanding the mechanisms responsible for regulating REM sleep (Pujol, Keane, and Jouvet 1978; Morgane 1981). Surely a knowledge of such interactions will improve our understanding of hallucinogenic drug states and schizophrenia as well. The recent finding that LSD, mescaline, psilocin, and DMT, but not lisuride or methysergide (a serotonin antagonist), are uniquely capable of facilitating the excitatory effects of serotonin and norepinephrine upon facial motoneurons (Aghajanian 1981) is intriguing. The currently popular activation-synthesis model of dreaming holds that dreams occur when certain pontine reticular cells (FTG cells) become excitable through the loss of serotoninergic and noradrenergic inhibitory influences (Hobson and McCarley 1977).

It is probable that dorsal raphe unit activity is mediated by tonic noradrenergic input and by self-regulatory serotonin autoreceptors (Aghajanian 1981). An agent which behaves as a specific autoreceptor antagonist might prevent the reduction of raphe unit firing which normally takes place during REM sleep and hallucinogenic drug states. Behavioral studies could clarify whether reduction in dorsal raphe activity plays an essential role in the psychological manifestations of these states. The basic analogy elaborated in this article dictates that a pharmacologic agent which can: (1) antagonize a biological mechanism which is common to hallucinogenic drug states and REM sleep; (2) attenuate the psychological effects of hallucinogens and suppress REM sleep (or reduce the primary process content of dreams) may be of potential benefit in the treatment of acute or incipient schizophrenia. It is hoped that continued research into the mechanisms of dreams and hallucinogenic drug states will augment research into the mechanisms of schizophrenia, and vice-versa. By understanding the similarities and differences between these three states, it may become possible finally to validate the comparisons made between them throughout the recorded history of philosophy and medicine.

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