BEHAVIORAL AND BRAIN SCIENCES (2000) **23,** 793–1121
Printed in the United States of America

Dreaming and REM sleep are controlled by different brain mechanisms

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Abstract: The paradigmatic assumption that REM sleep is the physiological equivalent of dreaming is in need of fundamental revision. A mounting body of evidence suggests that dreaming and REM sleep are dissociable states, and that dreaming is controlled by forebrain mechanisms. Recent neuropsychological, radiological, and pharmacological findings suggest that the cholinergic brain stem mechanisms that control the REM state can only generate the psychological phenomena of dreaming through the mediation of a second, probably dopaminergic, forebrain mechanism. The latter mechanism (and thus dreaming itself) can also be activated by a variety of nonREM triggers. Dreaming can be manipulated by dopamine agonists and antagonists with no concomitant change in REM frequency, duration, and density. Dreaming can also be induced by focal forebrain stimulation and by complex partial (forebrain) seizures during nonREM sleep, when the involvement of brainstem REM mechanisms is precluded. Likewise, dreaming is obliterated by focal lesions along a specific (probably dopaminergic) forebrain pathway, and these lesions do not have any appreciable effects on REM frequency, duration, and density. These findings suggest that the forebrain mechanism in question is the final common path to dreaming and that the brainstem oscillator that controls the REM state is just one of the many arousal triggers that can activate this forebrain mechanism. The "REM-on" mechanism (like its various NREM equivalents) therefore stands outside the dream process itself, which is mediated by an independent, forebrain "dream-on" mechanism.

Keywords: acetylcholine; brainstem; dopamine; dreaming; forebrain; NREM; REM; sleep

1. Introduction

It is well established that humans spend approximately 25% of sleeping hours in a state of paradoxical cerebral activation, accompanied by bursts of rapid eye movement (REM) and other characteristic physiological changes (Aserinsky & Kleitman 1953; 1955). This state occurs in roughly 90–100 minute cycles, alternating with four well-defined stages of quiescent sleep known as non-REM (NREM) sleep (see Rechtschaffen & Kales 1968 for standardized definitions). In 70–95% of awakenings from the REM state, normal subjects report that they have been dreaming, whereas only 5–10% of NREM awakenings produce equivalent reports (Dement & Kleitman 1957a; 1957b; Hobson 1988b).[1] These facts underpin the prevalent belief that the REM state is "the physiological concomitant of the subjective experience of dreaming" (LaBruzza 1978, p. 1537) and that dreaming is merely "an epiphenomenon of REM sleep" (Hobson et al. 1998b, p. R12). The discovery of the brainstem mechanisms that control REM sleep (Jouvet 1962; McCarley & Hobson 1975) has led to the further inference that the same mechanisms control dreaming.[2]

This target article presents a body of evidence that substantially contradicts these prevailing assumptions. This evidence demonstrates that, although there is an important link between REM sleep and dreaming, they are in fact doubly dissociable states (Teuber 1955). That is, REM can occur without dreaming and dreaming can occur without REM. The evidence reviewed here suggests also that these two states are controlled by different brain mechanisms. REM is controlled by cholinergic brainstem mechanisms whereas dreaming seems to be controlled by dopaminergic forebrain mechanisms. This unexpected dissociation between REM sleep and dreaming – and the brain mechanisms that regulate them – requires a major paradigm shift in sleep and dream science.

2. REM sleep is controlled by pontine brain stem mechanisms

The conclusion that Jouvet (1962) drew from his pioneering ablation, stimulation, and recording studies – namely that REM sleep is controlled by pontine brain stem mechanisms – remains central to all major contemporary models of sleep cycle control (for reviews, see Hobson et al. 1986; 1998b). The *reciprocal interaction model* of McCar-

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 0140-525X/00 $12.50

ley and Hobson (1975) has dominated the field over the past two decades. According to this model, REM sleep – and therefore dreaming – is triggered by cholinoceptive and/or cholinergic "REM-on" cells, and terminated by aminergic (noradrenergic and serotonergic) inhibitory "REM-off" cells. The REM-on cells are localized principally in the mesopontine tegmentum and the REM-off cells in the nucleus locus coeruleus and dorsal raphe nucleus (Fig. 1). Although it is acknowledged that the complete network of nuclei contributing to and giving effect to this oscillatory mechanism is more widely distributed than initial findings indicated (Hobson et al. 1986), executive control of the REM/NREM cycle is still localized narrowly within the pontine brain stem (Hobson et al. 1998b).[3] The assertion therefore remains that "cholinergic brainstem mechanisms *cause* REM sleep and dreaming" (Hobson 1988b, p. 202).

3. REM sleep is not controlled by forebrain mechanisms

An important corollary of the hypothesis that REM sleep – and therefore dreaming – is controlled by pontine brainstem mechanisms is the hypothesis that it is *not* controlled by forebrain mechanisms. Jouvet (1962) classically demonstrated that the forebrain is both incapable of generating REM sleep and unnecessary for the generation of REM sleep: when cortex is separated from brain stem, it no longer displays the normal cycle of REM activation (which is preserved in the isolated brainstem). It is still widely accepted that the forebrain is a passive participant in the REM state. Even the once-popular notion that the eye movements of REM sleep are attributable to forebrain "scanning" of visual dream imagery has been questioned (Pivik et al. 1977). The dominant view seems to be that the eye movements, their associated ponto-geniculo-occipital (PGO) waves, and the resultant imagery – in short, all the visual events of REM sleep – are initiated by brain stem neurons. The same applies to motor cortical events in REM sleep (Hobson 1988b; Hobson & McCarley 1977).

The brain stem localization of the mechanisms that regulate REM sleep physiology has become a springboard for far-reaching inferences about the mechanisms that regulate dream neuropsychology. An authoritative model of dream neuropsychology based on brain stem physiology is the *activation-synthesis model* (Hobson 1988b; Hobson & McCarley 1977). According to this model, which has dominated the field for the past two decades, dreams are actively generated by the brain stem and passively synthesized by the forebrain. The central tenet of this model is that the *causal* stimuli for dream imagery arise "from the pontine brain stem and not in cognitive areas of the cerebrum" (Hobson & McCarley 1977; p. 1347). The dream process is seen as having "no primary ideational, volitional, or emotional content" (p. 1347). Accordingly, the forebrain is assigned an entirely passive role: Its external input and output channels are blockaded by brain stem mechanisms, its perceptual and motor engrams are activated by brain stem mechanisms, and its memory systems merely generate "the best possible fit of [this] intrinsically inchoate data" (Hobson 1988b, p. 204). In this way it makes "the best of a bad job in producing even partially coherent dream imagery from the relatively noisy signals sent up from the brain stem" (Hobson & McCarley 1977, p. 1347).[4]

In the latest, admittedly speculative developments of this model (Hobson 1992; 1994; Hobson et al. 1998b), all the formal characteristics of dream psychology are accounted for by the above-described brainstem mechanisms. Dream hallucinosis, delusion, disorientation, accentuated affect, and amnesia are all attributed to the arrest of brain stem aminergic (noradrenergic and serotonergic) modulation of brainstem-induced cholinergic activation during REM sleep. It is even suggested that similar chemical mechanisms may underlie major psychotic symptoms that share formal features with dreaming (Hobson 1988b; 1992; 1994; Hobson & McCarley 1977). However, all of these propositions are questionable on several grounds.

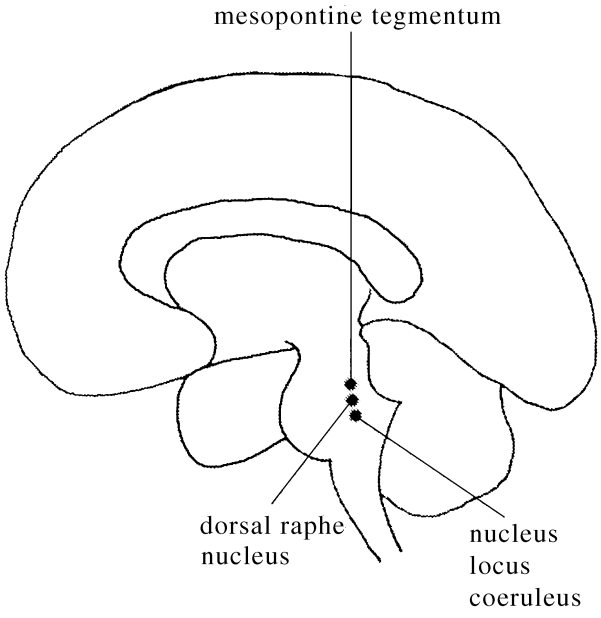

Figure 1. The major pontine brain stem nuclei implicated in REM/NREM sleep cycle control.

4. Not all dreaming is correlated with REM sleep

Dreaming and REM sleep are incompletely correlated. Between 5 and 30% of REM awakenings do not elicit dream reports; and at least 5–10% of NREM awakenings do elicit dream reports that are indistinguishable from REM reports (Hobson 1988b). The precise frequency of NREM dreaming is controversial. However, the principle that *REM can occur in the absence of dreaming and dreaming in the absence of REM* is no longer disputed (Hobson 1988b; 1992; cf. Vogel 1978a).

The original source of controversy was Foulkes's (1962) observation that complex mentation can be elicited in more than 50% of NREM awakenings (Foulkes 1962). Subsequent studies have confirmed this observation – and suggested that an average of 43% of NREM awakenings elicit such reports (Nielsen 1999) – but the extent to which the reported mentation may legitimately be described as "dreaming" is still disputed (cf. Cavellero et al. 1992). This is due to the fact that there are qualitative differences between NREM and REM dreams: In short, the *average* NREM dream is more "thoughtlike" than the average REM dream. This appears to reaffirm the view that the physio-

logical state differences between NREM and REM sleep are reflected in cognitive state differences between NREM and REM mentation. However, what is crucial for assessing the validity of the claim that dreaming is generated by the unique physiology of the REM state is not the question whether NREM "dreaming" occurs or not, but rather the extent to which NREM dreaming occurs that is *indistinguishable* from REM dreaming. This takes account of the problem of qualitative differences. It is generally accepted that NREM mentation that is indistiguishable from REM dreaming *does* indeed occur. Monroe et al.'s (1965) widely cited study suggests that approximately 10–30% of NREM dreams are indistinguishable from REM dreams (Rechtschaffen 1973). Even Hobson accepts that 5–10% of NREM dream reports are "indistinguishable by any criterion from those obtained from post-REM awakenings" (Hobson 1988b, p. 143). If we adjust this conservative figure to account for the fact that NREM sleep occupies approximately 75% of total sleep time, this implies that *roughly one quarter of all REM-like dreams occur outside of REM sleep.*

Moreover, REM-like NREM dreams are not randomly distributed through the sleep cycle; they cluster around specific NREM phases. As many as 50–70% of awakenings from sleep onset (descending NREM Stage I) yield reports that are not significantly different from REM dreams in all respects except for length (Foulkes et al. 1966; Foulkes & Vogel 1965; Vogel et al. 1972). Also, vivid REM-like reports are obtained with increasing frequency during the late NREM stages, in the rising morning phase of the diurnal rhythm (Kondo & Antrobus 1989).[5] This suggests that *these REM-like dreams are generated by specific NREM mechanisms.* In fact, within the reciprocal-interaction paradigm – where wakefulness and REM sleep are seen as terminal points on a continuum of aminergic demodulation – sleep onset and the rising morning phase have the opposite physiological characteristics to the REM state (Hobson 1992; 1994).

This is just one strand of the body of evidence that makes it difficult to retain the assumption that dreaming is generated by the unique physiological mechanism of the REM state.

In modifying the activation-synthesis model to accommodate these facts, the claim that all dreams are generated by the brain stem mechanisms that produce the REM state has recently been abandoned (Hobson 1992). This important shift in the dominant theory has passed almost unnoticed, however, because the closely related claim that all dreams are generated by *pontine brainstem* mechanisms has been retained (Hobson 1992; 1994). In the revised version of the activation-synthesis model (the Activation-Input-Mode [AIM] model), both REM *and* NREM dreams are attributed to reciprocal interactions between aminergic and cholinergic brainstem neurons (Hobson 1992; 1994). The formal characteristics of both REM *and* NREM mentation are therefore still described as "a function of the physiological condition of the reciprocally interacting brain stem neuronal populations that constitute the sleep-cycle control oscillator" (Hobson 1992, p. 228). Thus the doctrine of pontine brain stem control of dreaming has been retained, despite the fact that the assumption upon which it was explicitly based – the assumption of an isomorphism between REM sleep and dreaming (Hobson 1988b; 1992; Hobson & McCarley 1977) – has been disproved. The burden of evidence for the doctrine has thereby shifted from the phenomenological link between *REM sleep* and dreaming to the anatomical link between the *pontine brain stem* and dreaming.

5. Dreaming is preserved with pontine brain stem lesions

The assumption of an isomorphism between REM sleep and dreaming was important for the reason that the research program that isolated the brain mechanisms underlying REM sleep (ablation, stimulation, and recording studies) was conducted on infrahuman species in which concomitant effects on dreaming could not be monitored. The classical method for establishing brain-mind relationships in humans is the method of clinicoanatomical correlation in cases with naturally occurring lesions. If the assumption is correct that dreaming (like REM sleep) is controlled by brain stem mechanisms, it should be possible to demonstrate by this method that brainstem lesions in humans eliminate both REM sleep *and* dreaming.

Large lesions of the pontine brainstem eliminate all manifestations of REM sleep in domestic cats (Jones 1979), and this correlation has been confirmed in 26 human cases with naturally occurring lesions (Adey et al. 1968; Chase et al. 1968; Cummings & Greenberg 1977; Feldman 1971; Lavie et al. 1984; Markand & Dyken 1976; Osorio & Daroff 1980). However, elimination of REM (or near-elimination of REM) due to brainstem lesions was accompanied by cessation of dreaming in only one of these cases (Feldman 1971).[6] In the other 25 cases, the investigators either could not establish this correlation or they did not consider it (Adey et al. 1968; Chase et al. 1968; Cummings & Greenberg 1977; Lavie et al. 1984; Markand & Dyken 1976).[7]

Although cessation of dreaming has not been demonstrated in cases with elimination of REM due to brainstem lesions, the converse is also true: the preservation of dreaming in such cases has not been satisfactorily demonstrated (Solms [1997a] reported preserved dreaming in four patients with large pontine lesions, but polygraphic data was lacking). The paucity of evidence in this respect is at least partly due to the fact that pontine brain stem lesions large enough to obliterate REM usually render the patient unconscious (Hobson et al. 1998b).[8] Moreover, according to the revised version of the activation-synthesis model (the AIM model), dreaming is generated by both the REM and NREM components of the sleep-cycle control oscillator (Hobson 1992; 1994). This implies that dreaming can only be eliminated by very extensive brain stem lesions that obliterate *both* the REM and the NREM components of the oscillator. Such large lesions are almost certainly incompatible with the preservation of consciousness. It is therefore difficult to imagine how the assumption that dreaming is controlled by brainstem mechanisms can ever be refuted directly by lesion data. It can, however, be refuted indirectly via the corollary hypothesis that dreaming is not controlled by forebrain mechanisms. That is, the brain stem hypothesis would be falsified by clinicoanatomical methods if it could be demonstrated unequivocally that dreaming is eliminated by forebrain lesions that completely spare the brain stem.

6. Dreaming is eliminated by forebrain lesions which completely spare the brain stem

Subjective loss of dreaming due to a focal forebrain lesion was first reported more than 100 years ago. Wilbrand (1887; 1892) described a patient who dreamed "almost not at all anymore" (1887, p. 91) after suffering a bilateral occipital-temporal thrombosis. Müller (1892) documented a similar patient with bilateral occipital hemorrhages who "had no further dreams since her illness, whereas previously she not infrequently had vivid dreams and saw all sorts of things in them" (p. 868). Following these classical reports, 108 further cases with complete (or nearly complete) loss of dreaming in association with focal forebrain lesions have been published (Basso et al. 1980; Boyle & Nielsen 1954; Epstein 1979; Epstein & Simmons 1983; Ettlinger et al. 1957; Farah et al. 1988; Farrell 1969; Gloning & Sternbach 1953; Grunstein 1924; Habib & Sirigu 1987; Humphrey & Zangwill 1951; Lyman et al. 1938; Michel & Sieroff 1981; Moss 1972; Neal 1988; Nielsen 1955; Pena-Casanova et al. 1985; Piehler 1950; Ritchie 1959; Solms 1997a; Wapner et al. 1978). This clinicoanatomical correlation between subjective loss of dreaming and forebrain lesions has been confirmed repeatedly by the REM awakening method (Benson & Greenberg 1969; Brown 1972; Cathala et al. 1983; Efron 1968; Jus et al. 1973; Kerr et al.1978; Michel & Sieroff 1981; Murri et al. 1985) and by morning-recall questionnaires (Arena et al. 1984; Murri et al. 1984; 1985).[9]

In short, of the 111 published cases in the human neurological literature in which focal cerebral lesions caused cessation or near cessation of dreaming, *the lesion was localized to the forebrain – and the pontine brain stem was completely spared – in all but one case* (Feldman 1971). Critically, *the REM state was entirely preserved in all of the forebrain cases in which the sleep cycle was evaluated* (Benson & Greenberg 1969; Efron 1968; Jus et al. 1973; Kerr et al. 1978; Michel & Sieroff 1981). In view of the wide acceptance of the assumption that REM sleep is the physiological equivalent of dreaming, this lack of clinicoanatomical evidence correlating loss of REM sleep with loss of dreaming is striking.

The 110 published cases of loss of dreaming due to focal forebrain pathology fall into two anatomical groups (Fig. 2).[10] In 94 cases the lesion was situated in the posterior convexity of the hemispheres, in or near the region of the parieto-temporo-occipital (PTO) junction. The lesion was unilateral in 83 cases (48 left, 35 right) and bilateral in 11 cases. This localization has been confirmed repeatedly in substantial group studies (Arena et al. 1984; Cathala et al. 1983; Murri et al. 1984; 1985; Solms 1997a). In the other 16 cases, the lesion was situated in the white matter surrounding the frontal horns of the lateral ventricles. In these cases the damage was invariably bilateral. Of special interest is the fact that this lesion site coincides exactly with the region that was targeted in modified (orbitomesial) prefrontal leukotomy (Bradley et al. 1958). This association is confirmed by the fact that a 70–90% incidence of complete or nearly complete loss of dreaming was recorded in several large series of prefrontal leukotomy (Frank 1946; 1950; Jus et al. 1973; Partridge 1950; Piehler 1950; Schindler 1953). The many cases included in the latter series increases to almost 1,000 the number of reported cases of cessation of dreaming caused by focal forebrain lesions.

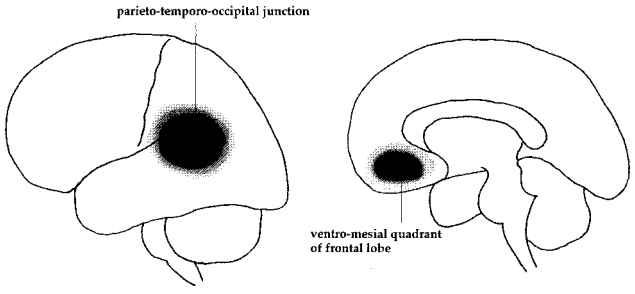

Figure 2. Lesion sites associated with loss of dreaming and preserved REM sleep.

7. Dreaming is actively generated by forebrain mechanisms

It is not surprising that dreaming is lost with lesions in the PTO junction – a region that supports various cognitive processes that are vital for mental imagery (Kosslyn 1994). But why should it be lost with lesions in the ventromesial quadrant of the frontal lobes?

This region contains substantial numbers of fibers connecting frontal and limbic structures with dopaminergic cells in the ventral tegmentum (Fig. 3). These circuits arise from cell groups situated in the ventral tegmental area of Tsai, where the source cells for the mesolimbic and mesocortical dopamine systems are situated. They ascend through the forebrain bundles of the lateral hypothalamus via basal forebrain areas (synapsing on many structures along the way, including nucleus basalis, bed nucleus of the stria terminalis, and shell of the nucleus accumbens) and they terminate in the amygdala, anterior cingulate gyrus, and frontal cortex. Descending components of this system probably arise from the latter brain areas, and there is reason to believe that they are influenced strongly by cholinergic circuits (Panksepp 1985).

This system is thought to have been the primary target of modified prefrontal leukotomy (Panksepp 1985). Its circuits instigate goal-seeking behaviors and appetitive interactions with the world (Panksepp 1985; 1998a). It is accordingly described as the "SEEKING" or "wanting" command

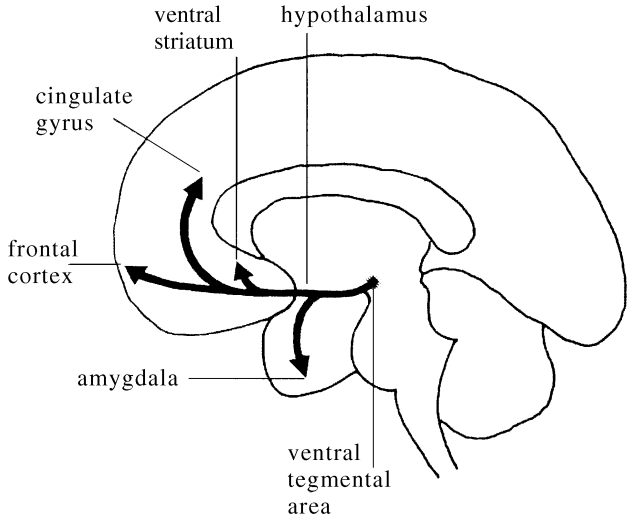

Figure 3. The mescortical/mesolimbic dopamine system.

system of the brain (Berridge, in press; Panksepp 1998a). It is considered to be the primary site of action of many stimulants (e.g., amphetamine and cocaine; see Role & Kelly 1991). The positive symptoms of schizophrenia – some of which can be artificially induced by l-dopa, amphetamines, and cocaine intoxication – are widely thought to result from overactivity of this system (Bird 1990; Kandel 1991; Panksepp 1998a). This system is also considered to be the primary site of action of antipsychotic medications (Role & Kelly 1991). A major psychological effect of antipsychotic therapy is loss of interactive interest in the world (Lehmann & Hanrahan 1954; Panksepp 1985). This underpins the popular view that antipsychotic medications – which block mesocortical-mesolimbic dopaminergic activity – yield "chemical leukotomies" (Breggin 1980; Panksepp 1985). Damage along this system produces disorders characterized by reduced interest, reduced initiative, reduced imagination, and reduced ability to plan ahead (Panksepp 1985). Lack of initiative or *adynamia* – where the patient does nothing unless instructed (Stuss & Benson 1983) – was a commonly observed side effect of orbitomesial prefrontal leukotomy (Brown 1985).

The following facts suggest that dreaming is generated by this dopamine circuit. First, dreaming ceases completely following transection of the forebrain component of this circuit (Frank 1946; 1950; Gloning & Sternbach 1953; Jus et al. 1973; Partridge 1950; Piehler 1950; Schindler 1953; Solms 1997a). These lesions have no effect on REM sleep. Transection or chemical inhibition of the same circuit reduces the positive symptoms of schizophrenia (Breggin 1980; Panksepp 1985), some formal features of which have long been equated with dreaming (Freud 1900; Hobson 1992; 1988b; Hobson & McCarley 1977). Second, adynamia (a common side effect of the surgical transection of this circuit) is a typical correlate of loss of dreaming following deep bifrontal lesions, and it statistically discriminates between dreaming and nondreaming patients with such lesions (Solms 1997a). Third, chemical activation of this circuit (e.g., through L-dopa) stimulates not only positive psychotic symptoms but also excessive, unusually vivid dreaming and nightmares (Nausieda et al. 1982; Scharf et al. 1978),[11] in the absence of any concomitant effect on the intensity, duration or frequency of REM sleep (Hartmann et al. 1980).[12] Fourth, drugs that block activity in this circuit (e.g., haloperidol) inhibit excessive, unusually frequent, and vivid dreaming (Sacks 1985; 1990; 1991) and other psychotic symptoms.

These facts suggest that the mesocortical-mesolimbic dopamine system plays a causal role in the generation of dreams. The relationship between this putative dopaminergic "dream-on" mechanism and the cholinergic REM-on mechanism of the reciprocal interaction model is discussed in the final section of this paper.

A further body of evidence strongly supports the view that dreaming can be *initiated* by forebrain mechanisms independently of the REM state. It is well established that nocturnal seizures – which typically occur during NREM sleep (Janz 1974; Kellaway & Frost 1983) – can present in the form of recurring nightmares[13] (Boller et al. 1975; Clarke 1915; De Sanctis 1896; Epstein 1964; 1967; 1979; Epstein & Ervin 1956; Epstein & Freeman 1981; Epstein & Hill 1966; Kardiner 1932; Naville & Brantmay 1935; Ostow 1954; Penfield 1938; Penfield & Erickson 1941; Penfield & Rasmussen 1955; Rodin et al. 1955; Snyder 1958; Solms 1997a; Thomayer 1897). In 22 of the 24 published cases of this type, the recurring nightmares were caused by epileptiform activity in the temporal lobe, that is, by an unequivocally *forebrain* mechanism. (In the other two cases, the nightmares were associated with epileptiform activity in another part of the forebrain: the parietal lobe.) The causal link between the epileptic activity and the recurring nightmares in such cases was demonstrated by Penfield and his coworkers (Penfield 1938; Penfield & Erickson 1941; Penfield & Rasmussen 1955), who were able to reproduce the same anxious experiences artificially (in the form of waking "dreamy state" seizures) by stimulating the temporal lobe focus. This causal link between the forebrain seizures and the recurring nightmares was confirmed (in Penfield's and other cases) by the fact that both the underlying seizure disorder and the nightmares responded to anticonvulsant therapy and/or anterior temporal lobectomy (Boller et al. 1975; Epstein 1964; 1967; 1979; Epstein & Ervin 1956; Epstein & Freeman 1981; Epstein & Hill 1966; Solms 1997a). These observations demonstrate conclusively that *dreaming can be initiated by forebrain mechanisms (which are unrelated to REM sleep) and terminated by forebrain lesions (which spare the REM cycle*).

8. Dreams are generated by a specific network of forebrain mechanisms

In the activation-synthesis model, dream imagery was attributed to nonspecific forebrain synthesis of chaotic brainstem impulses. This conception of the neuropsychological mechanisms underlying the formal characteristics of dream imagery is incompatible with recent clinicoanatomical and functional imagery findings (Braun et al. 1997; 1998; Solms 1997a). Data derived from these two methods have produced a remarkably consistent picture of the dreaming brain (Hobson et al. 1998b). Both the clinicoanatomical studies (Solms 1997a) and the functional imagery studies (Braun et al. 1997; 1998; Franck et al 1987; Franzini 1992; Heiss et al. 1985; Hong et al. 1995; Maquet et al. 1990; 1996; Madsen 1993; Madsen & Vorstrup 1991; Madsen et al. 1991a; 1991b; Nofzinger et al. 1997) suggest that dreaming involves concerted activity in a *highly specific* group of forebrain structures. These structures include anterior and lateral hypothalamic areas, amygdaloid complex, septal-ventral striatal areas; and infralimbic, prelimbic, orbitofrontal, anterior cingulate, entorhinal, insular, and occipitotemporal cortical areas (Braun et al. 1997; Maquet et al. 1996; Nofzinger et al. 1997). Primary visual cortex and dorsolateral prefrontal cortex are deactivated during REM dreaming (Braun et al. 1998). The role of the parietal operculum is uncertain (Heiss et al. 1985; Hong et al. 1995; Maquet et al. 1996).

This differentiated pattern of regional activation and inactivation mirrors some striking neuropsychological dissociations that have been reported in the clinicoanatomical literature. For example, unimodal abnormalities of visual dream imagery occur only with lesions in visual association cortex (Solms 1997a), but lesions in primary visual cortex have no effect on dreams. That is, visual dream imagery is intact in cortically blind patients (with V1/V2 lesions) whereas patients with irreminiscence who are unable to generate facial and color imagery in waking life (due to V4 lesions) also cannot generate faces or colors in their dreams

(Adler 1944; 1950; Botez et al. 1985; Brain 1950; 1954; Charcot 1883; Grunstein 1924; Kerr et al. 1978; Macrae & Trolle 1956; Sacks 1985; 1990; 1991; Sacks & Wasserman 1987; Solms 1997a; Tzavaras 1967). Dream imagery is similarly unaffected by primary cortical lesions in the other modalities. Hemiplegic patients (with unilateral perirolandic lesions) experience normal somatosensory and somatomotor imagery in their dreams (Brown 1972; 1989; Grünstein 1924; Mach 1906; Solms 1997a). Similarly, aphasic patients with left perisylvian lesions experience normal audioverbal and motor speech imagery in their dreams (Cathala et al. 1983; Schanfald et al. 1985; Solms 1997a). These findings suggest that somatosensory, somatomotor, audioverbal, and motor speech imagery in dreams are generated outside of the respective unimodal cortices for these classes of perceptual and motor imagery (probably in heteromodal paralimbic or PTO cortex). This implies that perceptual and motor dream imagery does not isomorphically reflect the simple activation of perceptual and motor cortex during sleep, as was claimed by the authors of the activation-synthesis model (Hobson 1988b; Hobson & McCarley 1977). It also suggests that dream imagery is not generated by chaotic activation of the forebrain. Rather, it appears that *specific forebrain mechanisms are involved in the generation of dream imagery* and that *this imagery is actively constructed through complex cognitive processes.*

In addition, a detailed analysis of the known forebrain mechanisms implicated in dreaming accounts empirically (Solms 1997a) for the formal characteristics of dreams – such as hallucination, delusion, disorientation, negative affect, attenuated volition, and confabulatory paramnesia – which were previously attributed speculatively (Hobson 1992; 1994) to the arrest of brain stem aminergic modulation during REM sleep. Lesions in anterior thalamus, basal forebrain, anterior cingulate, and mesial frontal cortex cause excessively vivid and frequent dreaming, a breakdown of the distinction between dreaming and waking cognition, and other reality-monitoring deficits. This suggests that the hallucinated, delusional, disoriented, and paramnestic quality of dream cognition may be associated with inhibition of these structures during sleep. Discharging lesions in medial and anterior temporal cortex cause recurring nightmares during sleep and unpleasant hallucinatory experiences during waking life. This suggests that the typical emotional and complex episodic qualities of dreams are produced through activation of these structures during sleep. It also suggests that these structures participate causally in the generation of at least some dreams. Bilateral lesions in the ventromesial frontal white matter cause complete cessation of dreaming in association with adynamia and other disorders of volitional interest. This suggests that these motivational mechanisms are essential for the generation of dreams. Lesions in dorsolateral prefrontal cortex cause disorders of volitional control, self-monitoring, and other executive deficits, but they have no effect on dreaming. This suggests that dorsolateral prefrontal cortex is inessential for dreaming sleep, which might explain the attenuated volition and other executive deficiencies of dream cognition (and further account for the defective self-monitoring). Right-sided lesions in the PTO junction cause complete cessation of dreaming in association with disorders of spatial cognition. This suggests that normal spatial cognition is essential for dreaming. It also suggests that the concrete spatial quality of dreams is supported by right hemispheric PTO activation. Lesions in the same region of the left hemisphere convexity also cause cessation of dreaming in association with disorders of quasi-spatial (symbolic) operations. This suggests that quasi-spatial cognition is equally essential for dreaming, and that this aspect of dreaming is contributed by left PTO activation. Lesions in ventromesial occipitotemporal (visual association) cortex cause unimodal deficits of dream imagery, in association with identical deficits of waking imagery. This suggests that the visual imagery of dreams is produced by activation during sleep of the same structures that generate complex visual imagery in waking perception. It also suggests that these structures are activated in dreams by heteromodal structures that are downstream of these unimodal visual processes during waking perception. Lesions in other unimodal cortices have no effect on dream imagery, notwithstanding their marked effects on waking perceptual and motor functions. This accounts for the predominantly visual quality of dream hallucinosis. It also suggests that the "backward projection" process which presumably generates visual dream imagery (Kosslyn 1994; Zeki 1993) does not extend further back than visual association cortex (V3).[14]

These evidence-based clinicoanatomical inferences (which tally very closely with the available functional imagery data) place the neuropsychology of dreaming on an equivalent footing with that of other cognitive functions. This finally paves the way for a testable theory of the brain mechanisms underlying the complex psychology of dreaming (Solms 1997a).

A noteworthy disparity between the clinicoanatomical and functional imagery data is the involvement of the pontine brain stem in dreaming sleep in some of the functional imaging studies (Braun et al. 1997; Maquet et al. 1996) but not the clinicoanatomical studies (Solms 1997a). This disparity is readily attributable to the fact that dreaming sleep was equated with REM sleep in the relevant imaging studies, which precluded the possibility of comparing dreaming with nondreaming NREM epochs (cf. Heiss et al. 1985). Imaging studies of the dreaming brain at sleep onset, or during the rising morning phase of the diurnal rhythm (when the brainstem mechanisms that generate REM are uncoupled from the putative forebrain mechanisms that generate dreaming), would be enlightening on this point.[15]

9. The relationship between dreaming and REM sleep reconsidered

The high correlation between the REM state and dreaming has traditionally been interpreted as indicating that the brain stem mechanisms that generate REM simultaneously generate dreaming (i.e., that the REM state is intrinsic to and isomorphic with dreaming). However, the data reviewed above suggest that REM and dreaming are in fact doubly dissociable states, in both normal and pathological conditions, and that they are controlled by different brain mechanisms. The high correlation between REM and dreaming therefore requires an alternative explanation.

Perhaps the most reasonable possibility is suggested by the observation that the various brain states that correlate with vivid dream reports all involve *cerebral activation during sleep.* The most common of these is the "paradoxical" state of REM, in which the brain is simultaneously asleep and highly activated. Dream reports are also correlated

with specific NREM states: descending Stage I (sleep onset) and the rising morning phase of the diurnal rhythm. These states are situated at polar ends of the sleep cycle, in the transitional phases between sleep and waking. The correlations between these states and dreaming have accordingly been interpreted as cerebral activation effects (Antrobus 1991; Hobson 1992). The same interpretation has been applied to the inverse correlation that exists between depth of NREM sleep (as measured by the sensory arousal threshold) and dreamlike mentation (Zimmerman 1970). Another state which triggers NREM dreaming is complex partial seizure activity, which could be described as a pathological form of cerebral activation during sleep. The fact that dreaming can be artificially generated by the administration of a variety of stimulant drugs, including both cholinergic[16] and dopaminergic agents, is open to a similar interpretation. Of crucial theoretical importance is the fact that dopaminergic agents increase the frequency, vivacity, and duration of dreaming without similarly affecting the frequency, intensity and duration of REM sleep (Hartmann et al. 1980). This observation, together with the equally important fact that damage to ventromesial frontal fibres obliterates dreaming but spares the REM cycle (Jus et al. 1973), suggests a specific dopaminergic dream-on mechanism that is dissociable from the cholinergic REM-on mechanism.

These observations show that dreaming is not an intrinsic function of REM sleep (or the brain stem mechanisms that control it). Rather, dreaming appears to be a consequence of various forms of cerebral activation during sleep. This implies a two-stage process, involving (1) cerebral activation during sleep and (2) dreaming. The first stage can take various forms, none of which is specific to dreaming itself, since reliable dissociations can be demonstrated between dreaming and all of these states (including REM). The second stage (dreaming itself) occurs only if and when the initial activation stage engages the dopaminergic circuits of the ventromesial forebrain. It is reasonable to hypothesize on this basis that these forebrain circuits are the final common path leading from various forms of cerebral activation during sleep (both REM and NREM) to dreaming per se. In this view, the high correlation between dreaming and the REM state merely reflects the fact that it is a regular and persistent source of cerebral activation during sleep. It is also possible that specific aspects of the REM state (e.g., noradrenergic and serotonergic demodulation) *facilitate* the primary dopaminergic effects. However, such facilitatory factors, which vary across the different sleep states associated with dreaming are not intrinsic to the dream process itself.

The biological function of dreaming remains unknown. This is at least partly attributable to the fact that the function of dreaming and the (equally unknown) function of REM sleep have been conflated for more than 40 years of research. Future studies of these functions should be uncoupled from one another. The statistical correlation between dreaming and REM sleep led early investigators to the understandable conclusion that they shared a single underlying mechanism. Subsequent research has demonstrated that this conclusion was erroneous: Dreaming and REM sleep are in fact doubly dissociable states, they have different physiological mechanisms, and in all likelihood they serve different functional purposes. The premise upon which the prevailing neuroscientific theories of dreaming were based has therefore lapsed. Progress in this area will now be hampered if we do not acknowledge our initial error, and resist the temptation to compress our expanding knowledge of the dreaming forebrain into the initial REM-based theoretical framework.

NOTES

1. Reported dream recall rates vary, depending not only on the method of awakening and interview but also on the investigator's definition of "dreaming" (Foulkes 1966). The figures cited here are conservative (they are discussed in more detail in sect. 4). There is no generally accepted definition of dreaming. For our purposes, dreaming may be defined as *the subjective experience of a complex hallucinatory episode during sleep.* However, what is more important than an absolute definition of dreaming in the present context is the relative frequency with which dream reports obtained from REM and NREM sleep are considered indistinguishable by blind raters.

2. *Control* in this context implies activate, generate, sustain, and terminate.

3. The concept of "executive control" (Hobson & McCarley 1977, p. 1338; Hobson et al. 1998b, p. R7) implies that the distributed network of structures that contribute to and give effect to the various physiological manifestations of the REM state are *recruited* and *coordinated* by a cholinergic/aminergic oscillator that is "centered" in the mesopontine tegmentum (Hobson 1988b, p. 185). Accordingly, Hobson proposes that "the *on-off switch* is the reciprocal-interacting neuronal populations comprising the aminergic neurons and the reticular neurons of the brain stem" (p. 205).

4. "If we assume that the physiological substrate of consciousness is in the forebrain, these facts completely eliminate any possible contribution of ideas (of their neural substrate) to the primary driving force of the dream process" (Hobson & McCarley 1977, p. 1338).

5. These dreams are difficult to distinguish from REM dreams. The following are illustrative examples. The first is a sleep-onset dream (descending Stage I):

> [It] had something to do with a garden plot, and I was planting seed in it. I could see some guy standing in this field, and it was kind of filled and cultivated, and he was talking about this to me. I can't quite remember what it was he did say, it seems to me as if it had to do with growing, whether these things were going to grow (Foulkes 1966, pp. 129–30).

The second example is a later NREM dream (25 minutes after the last REM episode):

> I was with my mother in a public library. I wanted her to steal something for me. I've got to try and remember what it was, because it was something extraordinary, something like a buffalo head that was in this museum. I had told my mother previously that I wanted this head and she said, all right, you know, we'll see what we can do about it. And she met me in the library, part of which was a museum. And I remember telling my mother to please lower her voice and she insisted on talking even more loudly. And I said, if you don't, of course, you'll never be able to take the buffalo head. Everyone will turn around and look at you. Well, when we got to the place where the buffalo head was, it was surrounded by other strange things. There was a little sort of smock that little boys used to wear at the beginning of the century. And one of the women who worked at the library came up to me and said, dear, I haven't been able to sell this smock. And I remember saying to her, well, why don't you wear it then? For some reason or other I had to leave my mother alone, and she had to continue with the buffalo head project all by herself. Then I left the library and went outside, and there were groups of people just sitting on the grass listening to music (Foulkes 1996, pp. 110–11).

6. This was a case of closed head injury with traumatic occlusion of the basilar artery. Autopsy and relevant radiological data were lacking. The distinct possibility of forebrain damage in this case cannot be excluded.

7. In one report (Osorio & Daroff 1980) two patients recalled no dreams when awoken during atypical NREM epochs; this is not unexpected and does not constitute evidence of loss of dreaming.

8. However, this is not always the case. At least eight patients with cessation or near-cessation of REM have been reported who were sufficiently conscious to communicate meaningfully with an examiner (Feldman 1971; Lavie et al. 1984; Markand & Dyken 1976; Osorio & Daroff 1979).

9. The possibility that the reported loss of dreaming in these patients is attributable to amnesia for dreams rather than true loss of dreams has been excluded not only by REM awakening but also by neuropsychological examination of memory functions in dreaming versus nondreaming patients (Solms 1997a).

10. This analysis excludes the "several" cases of cessation of dreaming after cerebral commissurotomy reported by Bogen (1969), whose findings have never been replicated (Greenwood et al. 1977; Hoppe 1977).

11. Excessive, unusually frequent, and vivid dreaming (of the type stimulated by dopamine agonists) has also been described in association with lesions of the anterior cingulate gyrus, basal forebrain nuclei and closely related structures (Gallassi et al. 1992; Gloning & Sternbach 1953; Lugaresi et al. 1986; Morris 1992; Sacks 1995; Solms 1997a; Whitty & Lewin 1957). Similar phenomena have been linked with central visual deafferentation (Brown 1972; 1989; Grünstein 1924; Hécean & Albert 1978; Solms 1997a). In some of these cases, dreaming occurs continuously throughout sleep (Gallassi et al. 1992; Gloning & Sternbach 1953; Lugaresi et al. 1986; Morris et al. 1992; Sacks 1995; Solms 1997a; Whitty & Lewin 1957). These patients are unable to distinguish between dreams and real experiences, and reality monitoring in general is disturbed (Solms 1997a). Most striking are cases in which waking thoughts spontaneously transform into complex hallucinatory experiences, resulting in confabulatory delusional states (Solms 1997a; Whitty & Lewin 1957). This disorder has been interpreted (Solms 1997a) as indicating that basal forebrain nuclei and closely related structures – which are known to participate in discriminative cognitive processes – play a critical role in distinguishing between thoughts and perceptions (i.e., inhibiting hallucinosis). Accordingly, damage to these mechanisms results in excessive dreaming during sleep (when the visual system is deafferented) and the intrusion of dreamlike mentation into waking thought.

It is reasonable to assume that the normal alternations between thoughtlike and dreamlike mentation that occur throughout the sleep cycle are somehow related to these (largely cholinergic) forebrain mechanisms. However, they appear to exert this influence *in the opposite direction to that predicted by the activation-synthesis hypothesis.* The fact that damage to cholinergic forebrain structures (i.e., *reduction* in cortical acetylcholine) produces *excessive* dreaming and dreamlike mentation is consistent with the widely held view that cortical acetylcholine enhances discriminative cognitive mechanisms (Perry & Perry 1995). Likewise, it is well known that *anti*cholinergic agents (e.g., scopolamine or atropine), acting on the muscarinic receptors which predominate in the basal forebrain, produce dreamlike mentation and complex hallucinations in awake subjects (Perry & Perry 1995). These effects are enhanced by eye closure. Therefore, if the REM state is indeed partly mediated by basal forebrain cholinergic mechanisms, as has recently been suggested by proponents of the reciprocal-interaction hypothesis (Hobson et al. 1998b), then something else must be added to the cholinergic activation in order to account for the occurence and formal characteristics of dreamlike mentation during this state. What is proposed here is that this "something else" is provided by the putative dopaminergic mechanism discussed above, the stimulation of which correlates positively with the generation of complex hallucinations, delusions, and other dreamlike phenomena.

12. In view of the importance of these findings in the present context, Hartmann et al.'s (1980) study is briefly summarized here: 13 subjects slept in the laboratory on four occasions each. They were awakened at the end of the first and second REM periods and either l-dopa (500 mg) or placebo were administered, so that the action of the l-dopa would coincide with the third REM period. A study lasting 52 nights yielded 128 dreams, of which 90 were postmedication (42 l-dopa and 48 placebo). Each dream was scored by four blind raters on five dream content scales: dreamlikeness, nightmarelikeness, vividness, emotionality, and detail. The l-dopa condition dreams were significantly more dreamlike ($p < 0.01$), vivid ($p < 0.01$), detailed ($p < 0.01$), and emotional ($p < 0.05$; t-test for correlated samples) than the placebo condition dreams. The two treatment conditions did not differ significantly on any polygraphic measures, including REM frequency, duration, and density.

13. These are subjective experiences of complex hallucinatory episodes, not night terrors. Here is an example:

> the patient [35 year old woman with idiopathic complex-partial seizures] reported a recurrent dream about her [dead] brother . . . which has reappeared several times. The dream is as follows: "I am walking down the street. I meet him. He is with a group of people whom I know now. I feel that I will be so happy to see him. I say to him, 'I'm glad you're alive,' but he'll deny that he is my brother and he'll say so, and I'll wake up crying and trying to convince him." (Epstein & Ervin 1956, p. 45)

Electroencephalography revealed a poorly defined right anterior temporal/right temporal spike focus, which appeared with the onset of drowsiness and light sleep.

14. This backward projection mechanism is apparently mediated in part by the cholinergic basal forebrain mechanism discussed previously.

15. The uncertain role of the parietal operculum in REM and NREM dreaming also awaits further investigation, but this question is unrelated to the main topic of the present paper.

16. Interesting to note, if cholinergic agents are administered prior to sleep onset they cause insomnia, if they are administered during NREM sleep they induce REM, and if they are administered during REM they provoke awakening (Sitaram et al. 1978b; Sitaram et al. 1976). This suggests a nonspecific activation-arousal effect.