Sleep and Dreaming

Scientific Advances and Reconsiderations

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How and why does the sleeping brain generate dreams?

Though the question is old, a paradigm shift is now occurring in the science of sleep and dreaming that is making room for new answers. From brainstem-based models of sleep cycle control, research is moving toward combined brainstem/forebrain models of sleep cognition itself. Furthermore, advances in philosophy, psychiatry, psychology, artificial intelligence, neural network modeling, psychophysiology, neurobiology, and clinical medicine make this a propitious time to review and bridge the gaps among these fields as they relate to sleep and dream research.

This book presents five papers by leading scientists at the center of the current firmament and more than seventy-five commentaries on those papers by nearly all the other leading authorities in the field. Topics include mechanisms of dreaming and REM sleep, memory consolidation in REM sleep, and an evolutionary hypothesis of the function of dreaming. The papers and commentaries, together with the authors' rejoinders, represent a huge leap forward in our understanding of the sleeping and dreaming brain, ultimately offering new and unique views of consciousness and cognition. They help provide new answers to both old and new questions, based on the latest findings in modern brain research. The book's multidisciplinary perspective will appeal to students and researchers in neuroscience, cognitive science, and psychology.

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Preface

For centuries there have been theories about how and why sleep occurs. Since the discovery of REM sleep in 1953, science has also asked how and why the individual stages of sleep, such as REM sleep and slow wave sleep, occur and what relationship they have with dreaming. The relationship of dreaming to brain physiology and neurochemistry, and the possible functions, or lack of functions, of REM sleep and of dreaming have also been addressed. This book highlights the current debates, disagreements, and understandings among many of the world's leading researchers, from many different disciplines, on these questions, including both theoretical and experimental work. The book comprises a collection of target chapters, commentaries, and replies to commentaries that were first published as a special issue on sleep and dreaming of the journal *Behavioral and Brain Sciences* in December 2000.

These are currently areas of great ferment. Fifty years ago dreams seemed to occur almost exclusively in REM sleep, a few years later dreams were also shown to occur in non-REM sleep, and the debate continues today about whether these stages of sleep result in different types of dreams or whether dreaming can occur in all stages of sleep and how closely characteristics of dreaming, such as the illogicality of some dreams or the ease with which they are forgotten, are tied to the physiology and neurochemistry of the brain. Theories of the function of dreams have abounded, from the clearing out of memories to the linking and forming of memories to creative problem-solving. There have also been theories of the function of REM sleep, such as of brain maturation in the newborn and the consolidation of memories at all ages. This book addresses theories of the possible functions and causes of dreaming and REM sleep, with implications not only for our knowledge of two activities that take up much of the human life span, but also for the study of the relationship of conscious experience to the brain and of the possible functions of consciousness.

The target chapters and commentaries give examples of a wide range of scientific methodologies that aim to address these issues, including the phenomenology and neuroscience of conscious states, cognitive performance testing, and the relationship of dream content to waking life events. The book makes clear the relevance of the study of dreaming to neuroscience, psychology, psychoanalysis, cognitive science, neurology, philosophy, psychiatry, and other fields, and we wish to thank all the authors and commentators from the many sciences involved for their participation in this book.

For this book version of the *Behavioral and Brain Sciences* special issue, an introduction and a postscript have been added that provide updates on relevant papers published during 2000, 2001, and 2002. The necessity for these updates shows the current rapid expansion of investigations into sleep and dreaming, along with the growth of neuroscience and the study of consciousness. We hope that this volume will inspire further experiments and debate concerning the relationships between dreaming and the sleeping brain and the functions of sleep and dreaming.

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Introduction

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The target chapters in this book address three issues in the science of sleep and dreaming: the relationship of dreaming to brain physiology and neurochemistry and the possible functions, or lack of functions, of REM sleep and of dreaming. The target chapters provide detailed summaries of previous work and a background to these current issues. This introduction aims to summarize the main claims of each of the target chapters and to cite recent papers of relevance to those chapters that appeared around the same time as or after the production of the *BBS* special issue. A further update, by Edward Pace-Schott, specifically on the neuroscience of sleep and dreaming, is provided at the end of the book.

The first three target chapters of this book are concerned with the relationship between dreaming and brain physiology and neurochemistry, with particular reference to the relationship of REM sleep to dreaming. Hobson, Pace-Schott, and Stickgold detail their AIM model of the mind-brain during dreaming and other states of consciousness. This model describes three dimensions of brain neuromodulation, these being level of brain activity (A), internal or external source of stimulation for cognition (I), and mode of organization of cognition (M), which they relate to aminergic/cholinergic balance. This chapter emphasizes the importance of REM sleep to dreaming, reviews the comparison of dreaming to waking cognition [of relevance here is Kahn et al. (2000) on how character recognition occurs during dreams], and, in common with Nielsen's target chapter, reviews the history of investigations into the quantitative and qualitative differences and similarities between dreams in REM and NREM sleep. Hobson et al. then review recent studies on neuroimaging of the brain during dreaming and sleep, which indicate increased activation of limbic, diencephalon, and brain stem areas during REM sleep and the decreased activation of these areas during NREM sleep. The original activation-synthesis model of Hobson and McCarley is then updated with recent work on the relationship of cholinergic enhancement, and serotonergic and noradrenergic suppression, to REM sleep; there are also additional details from recent findings on the manner in which aminergic and cholinergic systems exert their influences on the REM-NREM cycle.

The AIM state space model that evolved from the activation-synthesis model holds that not only is the brain activated (A) with low external input (I) during REM sleep but that the modulatory factor (M) is related to the deficiencies of logic and memory found in dreams. Since the *BBS* special issue, Fosse et al. (2001a) argue that their finding of the reciprocal variation in thoughts and hallucinations between wake, sleep onset, NREMS, and REMS indicates the need for the M factor, in addition to A and I. This method of comparing the prevalence and reciprocal covariance of different cognitive variables within each dream is also used in Fosse (2000), with a reply to the analysis by Nielsen (2000), and operationalizes the classification of different types of dreams, such as thoughtlike and hallucinatory dreams. Dream experiences have also recently been quantified in terms of four factors, Emotionality, Rationality, Activity, and Impression, using the Dream Property Scale of Takeuchi et al. (2001b), who found that EEG power in some frequencies is correlated with Rationality (the dream being more ordinary and orderly), and at other frequencies with Impression (the dream being more clear and focused), indicating some brain-mind isomorphism using a questionnaire method that is answered on awakening and is not mediated by the experimenter, nor, apparently, confounded by dream length.

Solms's target chapter details that REM sleep and dreaming are dissociable states, in that each can occur in the absence of the other; one reason for this is that, although there are average differences between NREM and REM dreams, 5–10% of NREM dreams are indistinguishable from REM dreams, in terms, for example, of their vivid and dramatic content. Using neuroanatomical studies, loss of dreaming is shown in this chapter to be associated with lesions to the ventro-mesial quadrant of the frontal lobe and to the parieto-temporal-occipital junction. The former area is known to be important for goal-seeking and appetitive behaviors, the latter area for supporting mental imagery. Solms concludes that dreaming is controlled by forebrain, probably dopaminergic, mechanisms whereas REM sleep is controlled by cholinergic brain stem mechanisms. [Gottesmann (2000) also hypothesizes that the release of dopamine results in the "psychotic-like" fantasies and irrational mental activities of dreaming.] REM sleep is therefore held to be one of many possible activators of forebrain dreaming mechanisms; others include descending stage 1 at sleep onset and the rising morning phase of the diurnal rhythm. For an update on the dopaminergic and cholinergic influences on dreaming the reader should see Solms (2002) and Cicogna & Bosinelli (2001) for more on the interaction between top-down and bottom-up components of dream mentation and for a consideration of what aspects of consciousness remain or are diminished in dreaming. Reiser (2001) suggests that top-down (psychological, psychoanalytic) and bottom-up (neuroscience) approaches to

dreaming and REM sleep are needed to account for the form and possible functions of dreams, with emotion being a bridge belonging to both domains. For example, to understand dreams one needs the top-down information derived from psychoanalysis of the dreamer's personal history and how it is incorporated into dreams together with the bottom-up PET studies of limbic areas that are activated during REM sleep.

Nielsen lists further examples where dreaming can occur in NREM sleep, such as when there is external sensory stimulation. He proposes that there are many levels of cognitive activity during sleep, from vivid intense dreams to thinking and fragmentary impressions to preconscious cognition, with the more complex or dramatic types of dreams more likely to occur in REM sleep. He shows that the liberalization (from around 1962) of what was accepted by dream researchers as a "dream" resulted in higher rates of dream recall being recorded from REM and NREM sleep and a diminution of the differences found between the dreams of the two states. The main purpose of the chapter is to review and reconcile evidence for the 1-generator view of dreaming, where similar processes of dream production are assumed to be occurring in REM and NREM sleep (but with the possibility that memory source activation and memory of dreams could be different in REM from NREM sleep), and the 2-generator view, where there are quantitative or qualitative differences between dreams from the two states. That the more vivid and even lucid types of dreams occur far more often in REM sleep is given as evidence for the 2-generator model.

Nielsen discusses, as do Hobson et al., the current debate about whether length of report should be controlled for in comparing dreams from REM and NREM sleep; such control has been found to eliminate almost all differences between dreams from the two states, but this statistical method is contentious because dream length may itself be a result of real differences in the characteristics of dreams from the two states. To explain why many dreams from NREM sleep are indistinguishable from REM sleep dreams, Nielsen then proposes that components of REM sleep can occur during NREM sleep but remain hidden ("covert") either because not all components are present at once, and so the sleep epoch is not scored as REM sleep, or because measures are not sensitive enough to detect the component. Nielsen proposes a probabilistic model whereby REM-like dreams can occur in NREM sleep during windows that are approximately 15 minutes prior to or following a REM period.

Of relevance to the discussion in these chapters of the comparison of dreams in REM and NREM sleep is a recent paper by Baylor and Cavallero (2001). In their reanalysis of three previously published studies they find that episodic memory sources occur significantly more often for NREM than REM dreams, and this stage effect remains even when report length is controlled for. Stickgold et al. (2001) found that dream report length increases with time in stage only for REM sleep, not for NREM sleep, and Takeuchi et al. (2001a) found that occurrence of dreams during sleep onset REM periods is related to amount of REM sleep, whereas occurrence of dreams during sleep onset NREM periods is related to number of arousals, but not to length of NREMS. However, note that Conduit et al. (2001) find that postsleep recall of events that occurred during NREM sleep is worse than for REM sleep, and that therefore dreaming may occur equally in NREM sleep as in REM sleep, but just not be remembered. Similarly, Cicogna et al. (2000) ascribe the difference they find in REM and SWS dream recall rates to a mnemonic deficit, claiming that mental experiences may be produced almost continuously during sleep, this being a 1-generator theory. They did find a greater intensity of emotions during REM sleep, but level of self-participation and awareness did not differ between the two stages, and two significant differences between the stages, in number of characters and number of emotions, disappeared when dream length was partialled out.

The emphasis in these three chapters is on finding physiological and neurochemical correlates that explain the recall, lack of recall, and form of dreams across different brain states. For a review of psychological variables that affect individual differences in dream recall, see Blagrove & Akehurst (2000). As an indication that individual differences in length of dream reports may be a result of state-independent differences in reporting style, Stickgold et al. (2001) found intersubject differences in REM report lengths were correlated with similar differences in NREM, sleep onset, and waking report lengths.

In their target chapter Vertes and Eastman argue against REM sleep having a memory consolidation role, claiming that animal REM deprivation studies are divided equally in showing REM deprivation does or does not disrupt learning/memory. They account for REM deprivation studies that do show deficits in learning/memory as being due to the stress of the deprivation procedure, and a recent report by Spiegel et al. (1999) does find endocrine, metabolic, and stress effects of sleep restriction in humans. Vertes and Eastman claim that the majority of human REM deprivation studies find minimal or no effects on learning/memory, and they review work in humans on the suppression of REM sleep by antidepressants in which there are no, or negligible, effects on learning/memory. As a further context to their review, there has been debate over whether sleep restriction to less than 5 hrs per night, which can eliminate some REM sleep but generally leaves SWS intact, results in only minor or in large and cumulative cognitive deficits (Dinges et al. 1997; Pilcher & Huffcutt 1996). As Vertes and Eastman state in their reply to the commentaries, a recent series of experiments has compared memory after a period of early sleep (in which SWS predominates) with memory after a period of late sleep (in which REMS predominates). Readers may consult Wagner et al. (2001) for a recent example. Vertes and Eastman propose that REM sleep has a function of periodically activating the brain following each period of slow wave sleep. This view is supported by Horne's (2000) view that REM sleep tones up the sleeping cortex. Horne also accounts for the post-REM deprivation phenomenon of REM rebound, often taken as an indication of the importance of REM sleep to the organism, as instead being due to a default condition of loss of inhibition of REM sleep by non-REM sleep. Horne concludes that REM has little advantage over wakefulness in providing cerebral recovery or memory consolidation and that it can occur as a default condition when wakefulness is temporarily unnecessary to the organism, as would occur in situations of boredom or satiation.

Revonsuo's target chapter argues that during dreaming we rehearse threat perception and threat avoidance and

that this mechanism has evolved because it increases the probability of reproductive success in threatening environments, such as those inhabited by ancestral humans. He argues that dreams may only infrequently act to solve intellectual problems (this being a current matter of debate, for example, Barrett 2001a, 2001b; Baylor 2001). He claims they do not have a function of solving emotional problems, as their function, like pain and fear, is to aid reproductive fitness rather than mental health or comfort, indeed Koethe and Pietrowsky (2001) find that nightmares induce anxiety and physical complaints.

One proposition that Revonsuo uses to arrive at his theory is that dreams are an organized and selective simulation of the perceptual world, that is, they are not random or disorganized or purely reflective of waking life. On his claim about dreams not being random, Stickgold et al. (1994) find sufficient coherence across dream reports for judges to distinguish intact from spliced reports. However, Roussy et al. (2000) demonstrate an inability of independent observers to detect a clear resemblance between participants' daily events and manifest dream content, although Revonsuo does note that in nonthreatening environments dreams may not show their threat simulation function. The evidence that dreams select for negative content is detailed in his chapter, such as the preponderance in dreams of misfortune over good fortune and the high frequency of aggressive strangers in dreams. Of relevance here is the finding of Bears et al. (2000), who, defining masochistic dreams as ones that involve negative self-representation, disappointment, loss, or lack or where the dreamer is lost, excluded, or ridiculed, report that depressed individuals tend to report masochistic dreams closer to morning than do nondepressed individuals, in whom masochistic dreams are equally distributed across the night. Revonsuo also proposes that waking threats activate the threat simulation system, and there is recent work relevant to this. The presence and intensity of the contextualizing (or central) images in dreams are higher among participants who report any abuse (physical or sexual, childhood or recent) compared to those who report no abuse (Hartmann et al. 2001). Furthermore, Zadra and Donderi (2000) found significant negative correlations between well-being and nightmare frequency and that the retrospective memory of frequency of nightmares and bad dreams greatly underestimates their frequency, in comparison to daily logs: a discussion of the directions of causality for the relationship between anxiety and disturbing dreams in adolescents is provided by Nielsen et al. (2000). Methodological problems with the assessment of emotions during dreams are described by Fosse et al. (2001b), who find that 74% of REM reports have at least one discrete emotion, and that the amount of positive or negative emotions in dreams does not change across the night.

Revonsuo then argues that stimulation of perceptual and motor skills during dreams, even when dreams are not explicitly remembered, leads to enhanced performance in waking life. On this point the theory is in accord with evidence that higher mental processes, such as those underlying social interaction, affect and evaluation, motivation and goal-setting, can occur without conscious choice or guidance (Bargh & Ferguson 2000). Revonsuo's view of the dream as an environment in which to act can be contrasted to the more metaphorical and symbolic view of dreaming (e.g., Lakoff 1993). Note, however, that Revonsuo states that other functions may also be possible for dreams. Recent suggestions are that dreams aid attachment for people who are insecurely attached (McNamara et al. 2001) and that pleasant or moderately unpleasant dreams may be sources of personal insight during dream interpretation (Zack & Hill 1998).

The five target chapters now follow. It is hoped that the debates over the relationship between dreaming and brain physiology, and over the memory consolidation function of REM sleep and the proposed threat simulation function of dreaming, will enhance the wider fields of neuroscience and of the study of the nature of consciousness and the specific questions of how and why we dream.

References

Bargh, J. A. & Ferguson, M. J. (2000) Beyond behaviorism: On the automatism of higher mental processes. *Psychological Bulletin* 126:925–45.

Barrett, D. (2001a) Comment on Baylor: A note about dreams of scientific problem solving. *Dreaming* 11:93–5.

Barrett, D. (2001b) *The committee of sleep: How artists, scientists and athletes use their dreams for creative problem solving.* Crown/Random House.

Baylor, G. W. (2001) What do we really know about Mendeleev's dream of the periodic table? A note on dreams of scientific problem solving. *Dreaming* 11:89–92.

Baylor, G. W. & Cavallero, C. (2001) Memory sources associated with REM and NREM dream reports throughout the night: A new look at the data. *Sleep* 24:165–70.

Bears, M., Cartwright, R. & Mercer, P. (2000) Masochistic dreams: A gender-related diathesis for depression revisited. *Dreaming* 10:211–19.

Blagrove, M. & Akehurst, L. (2000) Personality and dream recall frequency: Further negative findings. *Dreaming* 10:139–48.

Cicogna, P. & Bosinelli M. (2001) Consciousness during dreams. *Consciousness and Cognition* 10:26–41.

Cicogna, P., Natale, V., Occhionero, M. & Bosinelli, M. (2000) Slow wave and REM sleep mentation. *Sleep Research Online* 3:67–72. (http://www.sro.org/2000/Cicogna/67)

Conduit, R., Crewther, S. & Coleman, G. (2001) Poor recall of eye-movement signals from NREM compared to REM sleep: Implications for models of dreaming. *Sleep* 24 (Abstract supplement):A181.

Dinges, D., Pack, F., Williams, K., Gillen, K. A., Powell, J. W., Ott, G. E., Aptowicz, C. & Pack, A. I. (1997) Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. *Sleep* 20:267–77.

Fosse, R. (2000) REM mentation in narcoleptics and normals: An empirical test of two neurocognitive theories. *Consciousness and Cognition* 9:488–509.

Fosse, R., Stickgold, R. & Hobson, J. A. (2001a). Brain-mind states: Reciprocal variation in thoughts and hallucinations. *Psychological Science* 12:30–6.

Fosse, R., Stickgold, R. & Hobson, J. A. (2001b). The mind in REM sleep: Reports of emotional experience. *Sleep* 24:947–55.

Gottesmann, C. (2000) Hypothesis for the neurophysiology of dreaming. *Sleep Research Online* 3:1–4. (http://www.sro.org/2000/gottesmann/1/)

Hartmann, E., Zborowski, M., Rosen, R. & Grace, N. (2001) Contextualizing images in dreams: More intense after abuse and trauma. *Dreaming* 11:115–26.

Horne, J. A. (2000) REM sleep – by default? *Neuroscience and Biobehavioral Reviews* 24:777–97.

Kahn, D., Stickgold, R., Pace-Schott, E. F. & Hobson, J. A. (2000) Dreaming and waking consciousness: A character recognition study. *Journal of Sleep Research* 9:317–25.

Koethe, M. & Pietrowsky, R. (2001) Behavioral effects of nightmares and their correlations to personality patterns. *Dreaming* 11:43–52.

Lakoff, G. (1993) How metaphor structures dreams: The theory of conceptual metaphor applied to dream analysis. *Dreaming* 3:77–98.

McNamara, P., Andresen, J., Clark, J., Zborowski, M. & Duffy, C. A. (2001) Impact of attachment styles on dream recall and dream content: A test of the attachment hypothesis of REM sleep. *Journal of Sleep Research* 10:117–27.

Nielsen, T. A. (2000) Dream mentation production and narcolepsy: A critique. *Consciousness and Cognition* 9:510–13.

Nielsen, T. A., Laberge, L., Paquet, J., Tremblay, R. E., Vitaro, F. & Montplaisir, J. (2000) Development of disturbing dreams during adolescence and their relation to anxiety symptoms. *Sleep* 23:727–36.

Pilcher, J. J. & Huffcutt, A. I. (1996) Effects of sleep deprivation on performance: A meta-analysis. *Sleep* 19:318–26.

Reiser, M. F. (2001) The dream in contemporary psychiatry. *American Journal of Psychiatry* 158:351–9.

Roussy, F., Brunette, M., Mercier, P., Gonthier, I., Grenier, J., Sirois-Berliss, M., Lortie-Lussier, M. & De Koninck, J. (2000) Daily events and dream content: Unsuccessful matching attempts. *Dreaming* 10:77–83.

Solms, M. (2002). Dreaming: Cholinergic and dopaminergic hypotheses. In: *Neurochemistry of consciousness: Transmitters in mind*, ed. E. Perry, H. Ashton, & A. Young. John Benjamins Publishing Company.

Spiegel, K., Leproult, R. & Cauter, E. V. (1999) Impact of sleep debt on metabolic and endocrine function. *The Lancet* 354:1435–9.

Stickgold, R., Malia, A., Fosse, R. & Hobson, J. A. (2001) Brain-mind states: I. Longitudinal field study of sleep/wake factors influencing mentation report length. *Sleep* 24:171–9.

Stickgold, R., Rittenhouse, C. D. & Hobson, J. A. (1994) Dream splicing: A new technique for assessing thematic coherence in subjective reports of mental activity. *Consciousness and Cognition* 3:114–28.

Takeuchi, T., Miyasita, A., Inugami, M. & Yamamoto, Y. (2001a) Intrinsic dreams are not produced without REM sleep mechanisms: Evidence through elicitation of sleep onset REM periods. *Journal of Sleep Research* 10:43–52.

Takeuchi, T., Ogilvie, R. D., Ferrelli, A. V., Murphy, T. I. & Belicki, K. (2001b) The Dream Property Scale: An exploratory English version. *Consciousness and Cognition* 10:341–55.

Wagner, U., Gais, S. & Born, J. (2001) Emotional memory formation is enhanced across sleep intervals with high amounts of rapid eye movement sleep. *Learning and Memory* 8:112–19.

Zack, J. S. & Hill, C. E. (1998) Predicting outcome of dream interpretation sessions by dream valence, dream arousal, attitudes towards dreams, and waking life stress. *Dreaming* 8:169–85.

Zadra, A. & Donderi, D. C. (2000) Nightmares and bad dreams: Their prevalence and relationship to well-being. *Journal of Abnormal Psychology* 109:273–81.

Dreaming and the brain: Toward a cognitive neuroscience of conscious states

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Abstract: Sleep researchers in different disciplines disagree about how fully dreaming can be explained in terms of brain physiology. Debate has focused on whether REM sleep dreaming is qualitatively different from nonREM (NREM) sleep and waking. A review of psychophysiological studies shows clear quantitative differences between REM and NREM mentation and between REM and waking mentation. Recent neuroimaging and neurophysiological studies also differentiate REM, NREM, and waking in features with phenomenological implications. Both evidence and theory suggest that there are isomorphisms between the phenomenology and the physiology of dreams. We present a three-dimensional model with specific examples from normally and abnormally changing conscious states.

Keywords: consciousness, dreaming, neuroimaging, neuromodulation, NREM, phenomenology, qualia, REM, sleep

1. Introduction

Dreaming is a universal human experience that offers a unique view of consciousness and cognition. It has been studied from the vantage points of philosophy (e.g., Flanagan 1997), psychiatry (e.g., Freud 1900), psychology (e.g., Foulkes 1985), artificial intelligence (e.g., Crick 1994), neural network modeling (Antrobus 1991; 1993b; Fookson & Antrobus 1992), psychophysiology (e.g., Dement & Kleitman 1957b), neurobiology (e.g., Jouvet 1962) and even clinical medicine (e.g., Mahowald & Schenck 1999; Mahowald et al. 1998; Schenck et al. 1993). Because of its broad reach, dream research offers the possibility of bridging the gaps in these fields.

We strongly believe that advances in all these domains make this a propitious time to review and further develop these bridges. It is our goal in this target article to do so. We will study dreams (defined in the American Heritage Dictionary [1992] as "a series of images, ideas, emotions, and sensations occurring involuntarily in the mind during certain stages of sleep") and REM sleep, as well as the numerous forms of wake-state and sleep-state mentation. We will also review polysomnographically defined wake and sleep states. Our analyses will be based on comparisons and correlations among these various mental and physiological states.

1.1. An integrative strategy

Three major questions seem to us to be ripe for resolution through constructive debate:

1. Are the similarities and differences in the conscious experiences of waking, NREM, and REM sleep defined with sufficient clarity that they can be measured objectively? If so, do the measures establish clear-cut and major differences between the phenomenological experience of these three physiological states?
2. Are the similarities and differences between the brain

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substrates of the states of waking, NREM, and REM sleep defined with sufficient clarity that they can be measured objectively? If so, do the measures establish clear-cut differences between these states at the level of brain regions, as well as at the cellular and molecular levels?

3. To the extent that affirmative answers can be given to the two preceding questions, can a tentative integration of the phenomenological and physiological data be made? Can models account for the current results and suggest experiments to clarify remaining issues?

Hoping to stimulate a useful debate, we will answer all three of the preceding questions affirmatively, documenting our responses with appropriate data drawn from our own work and from that of our colleagues. Referring to this ample literature, one can now identify numerous operationally defined psychological and physiological parameters with which to make such conscious state comparisons. In developing our answers, we will advance the thesis that the conscious states of waking, NREM, and REM sleep differ in three clear and important ways which are measurable at both the psychological and physiological levels. The three parameters will become the axes of a state space model that we introduce only briefly here but discuss in more detail in concluding this article.

1.2. A state space model of the brain-mind

In essence, our view is that the brain-mind is a unified system whose complex components dynamically interact so as to produce a continuously changing state. As such, any accurate characterization of the system must be multidimensional and dynamic and must be integrated across the neurobiological and psychological domains. Both neurobiological and psychological probes of the system must therefore be designed, applied and interpreted so as to recognize and clarify these features.

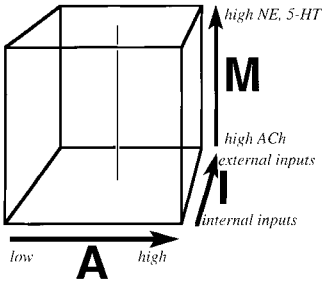
As a first step in that direction, we have created a three-dimensional state space model (AIM) that allows us to represent the system according to variables with referents in both the neurobiological and psychological domains as is shown in Figure 1. They are activation (A), information flow (I), and mode of information processing (M). Each of these terms has meaning both at the cognitive and neurobiological levels.

Roughly speaking, these dimensions are meant to capture respectively: (1) the information processing capacity of the system (activation); (2) the degree to which the information processed comes from the outside world and is or is not reflected in behavior (information flow); and (3) the way in which the information in the system is processed (mode).

The resulting state space model, while still necessarily overly simplistic, is nonetheless a powerful tool for studies of consciousness. It captures many aspects of the neurobiological, cognitive, and psychological dynamics of wake-sleep states, and is unique in several important respects that we will discuss in light of the controversial conceptual and empirical issues that have stymied the study of waking, sleeping, and dreaming.

1.3. Caveat lector

In setting the stage for a full explication of our integrative AIM model (sect. 4), we will review the evidence regarding the differentiation of brain-mind states at the levels of psychophysiology (sect. 2) and basic and clinical neuroscience



Model Factor	Psychological	Neurobiological
A-Activation: Level of energy processing capacity	•Word count •Cognitive complexity e.g., perceptual vividness, emotional intensity, narrative	•EEG activation •Firing level and synchrony of reticular, thalamic and cortical neurons
I-Information Source internal or external.	•Real world space, time and person referents and their stability •Real vs. imagined action	•Level of presynaptic and postsynaptic inhibition. •Excitability of sensorimotor pattern generators.
M-Mode: Organization of data.	•Internal consistency? •Physical possibility? •Linear logic?	•Activity level of aminergic neurons

Figure 1. The Activation-Input Source-Neuromodulation model (AIM). Illustration of three dimensional state space and the psychological neurobiological correlates of each dimension. See section 4 and also Hobson (1990; 1992a; 1997a).

(sect. 3). Although these reviews are extensive, they do not broach many of the fundamental questions of sleep research. For example, we do not consider the biological functions of REM sleep as we do elsewhere (Hobson 1988a) nor do we address the equally interesting question of how psychological and cognitive factors impinge upon sleep neurobiology, a subject which has been the focus of our most recent work (Stickgold et al. 1998a; 1999a; 2000a; Xie et al. 1996). As has often been shown, cognitive activity affects sleep as well as vice versa (e.g., Smith & Lapp 1991) reflecting, certainly, a reciprocal effect of psychological factors and their neural substrates. Additionally, we sidestep entirely the intriguing but difficult issue of whether dreaming itself, as a conscious experience, has a psychological function over and above the postulated benefits of sleep to homeostasis and heteroplasticity (Hobson 1988a). Finally, it is important to note that we deal here exclusively with what Chalmers (1995b) has termed the "easy problem" of consciousness, that is, the mechanisms of the cognitive components of consciousness, rather than the "hard problem" of how consciousness itself could arise from a neural system (see, e.g., Tononi & Edelman 1998; Woolf 1997).

2. The phenomenology and psychophysiology of waking, sleeping, and dreaming

In this section we discuss the evidence which has been gathered over the past 40 years in an effort to define the conscious states of waking, sleeping, and dreaming and to measure their formal features quantitatively. With respect to the first question raised by us in the introduction, we will defend the position that these three states *can* be defined, that their components can be analyzed and measured, and that they *are* significantly different from one another.

After presenting our justification for this claim, we will

address the claim made by many psychologists that differences between REM and NREM mentation – and even differences between REM and waking mentation – are much smaller than we believe. In the course of this discussion, we will identify several areas of disagreement and then suggest some new approaches to their resolution.

Definitions of dreaming have ranged from the broadest "any mental activity occurring in sleep" to the narrower one that we prefer:

> Mental activity occurring in sleep characterized by vivid sensorimotor imagery that is experienced as waking reality despite such distinctive cognitive features as impossibility or improbability of time, place, person and actions; emotions, especially fear, elation, and anger predominate over sadness, shame, and guilt and sometimes reach sufficient strength to cause awakening; memory for even very vivid dreams is evanescent and tends to fade quickly upon awakening unless special steps are taken to retain it.

We believe that this highly specified definition serves both folk psychology and cognitive neuroscience equally well. It captures what most people mean when they talk about dreams and it lends itself admirably to neurocognitive analysis as we now intend to show.

2.1. Early findings of distinct differences between REM and NREM mentation

Before proceeding, we provide definitions of "REM" and "NREM" sleep for those readers unfamiliar with these terms. These two clearly distinguishable types of sleep are defined, by convention, in terms of electrophysiological signs detected with a combination of electroencephalography (EEG), electroculography (EOG), and electromyography (EMG) whose measurement is collectively termed "polysomnography" (see Rechtschaffen & Kales 1968). First described by Aserinsky and Kleitmann in 1953, REM sleep (also known as "paradoxical," "active" or "desynchronized" sleep) is characterized by: (1) wake-like and "activated" (high frequency, low amplitude or "desynchronized") activity in the EEG; (2) singlets and clusters of rapid eye movements (REMs) in the EOG channel; and (3) very low levels of muscle tone (atonia) in the EMG channel. NonREM (NREM) sleep includes all sleep apart from REM and is, by convention, divided into four stages corresponding to increasing depth of sleep as indicated by the progressive dominance of the EEG by high-voltage, low-frequency (also termed "synchronized") wave activity. Such low frequency waves dominate the deepest stages of NREM (stages 3 and 4) which are also termed "slow-wave" or "delta" sleep. We refer the reader to Hobson (1989) for a comprehensive primer on sleep physiology.

Aserinsky and Kleitman's (1953) report of the correlation of REM sleep with dreaming began an intense period of research on the relation of brain to mind that lasted well into the 1970s. In the early days of the human sleep-dream laboratory era, much attention was paid to the specificity, or lack thereof, of the REM-dream correlation using the newly available sleep laboratory paradigm. Normal subjects, usually students, were awakened from either the NREM or REM phase of sleep in the sleep laboratory and asked to report their recollection of any mental experience preceding the awakening.

During this period, the similarities and differences in mentation between the brain states of waking, NREM, and REM sleep were lavishly documented (e.g., Foulkes 1962; Foulkes & Fleisher 1975; Goodenough et al. 1959; Herman et al. 1978; Monroe et al. 1965; Nielsen 1999; Pivik & Foulkes 1968; Rechtschaffen 1973; Rechtschaffen et al. 1963; Vogel 1991). We have summarized these REM-NREM differences in Table 1. Some of the important conclusions from this cross-sectional normative paradigm are:

1. Following REM sleep awakenings, variously defined dream reports are obtained much more frequently (Aserinsky & Kleitman 1953; 1955; Dement 1955; Dement & Kleitman 1957b; Kales et al. 1967; Wolpert & Trosman 1958) or at least substantially more frequently (Foulkes 1962; Goodenough et al. 1965a; Hobson et al. 1965; Molinari & Foulkes 1969; Rechtschaffen et al. 1963; Stoyva 1965) than after NREM awakenings. For reviews of this early work see Foulkes (1966; 1967), Herman et al. (1978), Nielsen (1999), Pivik (1991), Rechtschaffen (1973), and Snyder (1967). In an extensive review of 29 REM and 33 NREM recall rate studies, Nielsen (1999) found an average REM recall rate of 81.8 (±8.7)% compared to an average rate for NREM of 42.5 (±21.0)%.

2. The frequency of dream recall rapidly drops off as awakenings are delayed beyond the end of a REM period (Dement & Kleitman 1957b; Goodenough et al. 1965b; Wolpert & Trosman 1958), a finding which has recently been both supported (Stickgold et al. 1994a) and challenged (Rosenlicht et al. 1994). Subjects who are able to indicate that they are dreaming during sleep more often indicate dreaming during REM than during NREM (Antrobus et al. 1965).

3. There exists a positive relationship of both report word count and subjectively estimated dream duration with the length of preceding REM sleep (Dement & Kleitman 1957b) and this relationship has been recently replicated for word count (Stickgold et al. 1994a). Moreover, stimulus-incorporation studies suggest that there exists a positive relationship between the length of time dream events would occupy in real time and the duration of the preceding REM sleep epoch (Dement & Wolpert 1958).

4. Judges are able to distinguish unaltered REM mentation reports from NREM reports (Monroe et al. 1965), a finding that has been recently replicated (e.g., Herman et al. 1978; Reinsel et al. 1992). Furthermore, some dreamers can subjectively determine whether they themselves had been awakened from REM or from NREM (Antrobus & Antrobus 1967).

5. Reports from REM sleep awakenings are typically longer (Antrobus 1983; Casagrande et al. 1990; 1996b; Foulkes & Rechtschaffen 1964; Foulkes & Schmidt 1983; Stickgold et al. 1994a; Waterman et al. 1993), more perceptually vivid, more motorically animated, more emotionally charged, and less related to waking life than NREM reports (Antrobus et al. 1987; Cavallero et al. 1992; Foulkes 1962; Herman et al. 1978; Ogilvie et al. 1982; Rechtschaffen et al. 1963; see Nielsen, 1999 and Table 1 for summaries). In addition, there is linguistic evidence for greater consolidation of dream elements in REM (Salzarulo & Cipolli 1979).

6. In contrast to REM reports, NREM reports contain thought-like mentation and representations of current concerns more often than do REM sleep reports (Foulkes 1962; Rechtschaffen et al. 1963).

In a review of early data, Monroe et al. (1965) stated that "the high degree of success attained by the judges [in dis-

Table 1. *Phenomenological differences between REM and NREM dream reports*

Study Sleep Stage	# S's	# S's x # nights	# awak- enings	% recall (any content)	% using more strict criteria	report length	bizarreness	visual vividness	emotionality	movement
Antrobus (1983)	73	73			not compared	no data given	not compared	REM vs St. 2	not compared	not compared
REM			73	no report		REM >St.2		n.s. when length		
St. 2 NREM			73	no report		p<.01		controlled		
Aserinsky & Kleitman (1953)	10	14			"dreaming"					
REM			27	74	74					
NREM			19	22	11					
Casagrande et al. (1996)	20	40			"≥1 sentence	*using word*	*w. Antrobus et*	*w. Antrobus et*	not compared	not compared
REM				REM	& ≥1 action"	*count indices:*	*al., 1976 index:*	*al., 1976 index:*		
early (in night)			40	early	75	early:	early:	early:		
late (in night)			40	late	75	REM> 2 & SO	REM> 2 & SO	REM> 2 & SO		
NREM (St. 2 abbreviated "2")				NREM (2)		late:	late:	late:		
early			40	early	50	REM & 2> SO	REM & 2> SO	REM & 2> SO		
late			40	late	70		*using a global*	*using a global*		
Sleep onset NREM St. 2 (SO)				NREM (SO)			*rating:*	*rating:*		
early			40	early	50		REM always >	REM always >		
late			40	late	55		2 & SO	2 & SO		
Cavallero et al. (1992)	60	120			not compared	temporal units	implausibility	not compared	% containing	not compared
REM			60	89.2		5.1	34 n.s.		62	
St. 3&4 NREM			60	64.5		1.88 p<.0001	50		34 p<.01	
Cicogna et al., 1998					not compared	temporal units	implausibility*	not compared	number reported	body feelings
late spontaneous REM	36	72	144	95		7.3	84.2%		.76	21.1%
late spontaneous St. 2			144	91		6.0	79.6%		.60	10.2%
Dement (1955)	13	?		not compared	"dreaming"	not compared	not compared	not compared	not compared	not compared
REM			51		88.2					
NREM			19		0					
Dement & Kleitman (1957)	9	61		not compared	"dreaming"	not compared	not compared	not compared	not compared	not compared
REM			191		79.6					
NREM			160		6.9%					

Foulkes (1962)	8	56			"vs. thinking"		judged scene	judged visual	judged present	judged present
REM			108	87	82		shift:REM>	vs. not:REM>	/absent: REM>	/absent: REM>
NREM			136	74	54		NREM $p<.02$	NREM $p<.02$	NREM $p<.02$	NREM $p<.01$
St. 1 NREM			32	69	56	subject-judged:	subject-judged	subject-judged	subject-judged	subject-judged
St. 2 NREM			32	74	51	REM>NREM	"distortion":	"% visible":	"present":	"activity":
St. 3&4 NREM			32	70	51	$p<.05$	R>N $p<.05$	R>N $p<.05$	R>N $p<.05$	R>N $p<.05$
Foulkes & Rechtschaffen (1964)	24	48			not compared	word count	subject-judged	subject-judged	subject-judged	subject-judged
REM			143	88.8		229.2	REM>NREM	REM>NREM	REM>NREM	REM>NREM
NREM			84	61.9		158.6	$p=.01$	$p=.01$	$p=.01$	$p=.01$
Foulkes & Schmidt (1983)	23	69			>1 temporal unit	temporal units	not compared	not compared	not compared	not compared
REM			82	93	80	5.5				
NREM			78	67	40	1.33 $p<.01$				
Goodenough et al. (1959)	16	48			not compared	not compared	not compared	not compared	not compared	not compared
REM			91	69.2						
NREM			99	34.3						
Goodenough et al. (1965a)	10	98			"dreaming"	word count	judged:	judged visual	not compared	judged activity:
REM			120	84	76	115	REM > NREM	imagery:REM		REM > NREM
NREM			240	45	21	34	$p<.02$	>NREM $p<.01$		$p<.01$
Hobson et al. (1965)	10	40–60			"dreaming"	not compared	not compared	not compared	not compared	not compared
REM			195	87.2	76.4					
NREM			102	37.2	13.7					
Kales et al. (1967)	3	40		dream+thinking	"dreaming"	not compared	not compared	not compared	not compared	not compared
REM			134	83	81					
NREM			108	35	7					
Kamiya (1961)	25	250			"dreaming"	not compared	not compared	not compared	not compared	not compared
REM			?	?	85					
NREM			400	46	27					
Molinari & Foulkes (1969)	10	40		tonic / phasic	not compared	not compared	not compared	subject judged	not compared	not compared
REM			40	80 100				tonic / phasic		
				descend / ascend				60 100		
NREM			79	72 75				79–80		
Ogilvie et al. (1982)	9	27		not reported	not reported	not compared	judged: REM>	judged: REM>	judged: REM>	not compared
REM			54				St. 2 NREM	St. 2 NREM	St. 2 NREM	
NREM			54				$p<.05$	"marginally"	"tendency"	

(*continued*)

Table 1. (*Continued*)

Study Sleep Stage	# S's	# S's x # nights	# awak- enings	% recall (any content)	% using more strict criteria	report length	bizarreness	visual vividness	emotionality	movement
Pivik & Foulkes (1968)	20	40			not compared	not compared	not compared	not compared	not compared	not compared
NREM total			158	64.6						
NREM St. 2			74	71.6						
NREM St. 3			56	64.3						
NREM St. 4			28	46.4						
Rechtschaffen et al. (1963)	17	30			Ss say dreaming	not compared	subject judged	subject judged	subject judged	not compared
REM				86	87		37% bizarre	74% vivid	74% emotional	
NREM				23	41		6% bizarre	24% vivid	24% emotional	
Salzarulo & Cipolli (1979)	8	80			"contentful"	# sentences	not compared	not compared	not compared	not compared
REM			240		95	4.22				
NREM			240		85	3.48				
Stickgold et al. (1994) Nightcap	11	110	(spont.)		> 100 words		not compared	not compared	not compared	not compared
REM			88	83	62	314				
NREM			61	54	18	65				
Stoyva (1965)	7 (deaf)	28			not compared	not compared	not compared	not compared	not compared	not compared
REM			51	73						
NREM			68	38						
Waterman et al. (1993)	12	24	72	not reported	not reported	REM>NREM	not compared	*w.Antrobus et al., 1976 index and length partialed out: REM>NREM*	not compared	not compared
Wolpert & Trosman (1958)	10	51			"dreaming"	not compared	not compared	not compared	not compared	not compared
REM			54	90.8	85.2					
NREM St. 2			26	3.8	0					

*Cicogna et al. 1998 actually found significantly more "space-time distortions" and a trend toward more "dimensional distortions" in Stage 2 versus REM reports, while the trend in global bizarreness (implausibility) went in the usual REM>Stage 2 direction. R = REM, N = NREM, spont. = spontaneous awakenings from identified sleep stage.

tinguishing REM from NREM reports] indicates that physiological sleep phase, REM or NREM, is highly diagnostic of the presence, amount, and quality of reported sleep mentation" (p. 456). In discussing the findings of this study, Rechtschaffen (1973) concluded that "these figures – discriminability ranging from about 70 to 90% – probably represent one of the best correlations ever discovered between psychological and physiological variables" (p. 163).

In REM sleep, the integrated conscious experience that is commonly referred to as dreaming is characterized by the following remarkably consistent set of features (see Hobson 1988b; 1994 for reviews):

1. Dreams contain formed hallucinatory perceptions, especially visual and motoric, but occasionally in any and all sensory modalities (Hobson 1988b; McCarley & Hoffman 1981; Snyder 1970; Zadra et al. 1998).

2. Dream imagery can change rapidly, and is often bizarre in nature (Hobson 1988b; 1997b; Hobson & Stickgold 1994a; Hobson et al. 1987; Mamelak & Hobson 1989a; McCarley & Hoffman 1981; Porte & Hobson 1986; Reinsel et al. 1992; Revonsuo & Salmivalli 1995; Williams et al. 1992). It has also been noted that dream reports contain a great many images and events which are relatively commonplace in everyday life (Dorus et al. 1971; Snyder 1970).

3. Dreams are delusional; we are consistently duped into believing that we are awake unless we cultivate lucidity (Barrett 1992; Hobson 1997b; Kahan 1994; LaBerge 1990; 1992; Purcell et al. 1986).

4. Self-reflection in dreams is generally found to be absent (Rechtschaffen 1978) or greatly reduced (Bradley et al. 1992) relative to waking and, when present, often involves weak, post hoc, and logically flawed explanations of improbable or impossible events and plots (Hobson 1988b; Hobson et al. 1987; Williams et al. 1992). It has been recently asserted, however, that self-reflection, self control and other forms of metacognition are more common in dreams than previously thought (Kahan 1994; Kahan & LaBerge 1994).

5. Dreams lack orientational stability; persons, times, and places are fused, plastic, incongruous and discontinuous (Hobson 1988b; 1997b; Hobson et al. 1987; McCarley & Hoffman 1981; Revonsuo & Salmivalli 1995; Rittenhouse et al. 1994; Stickgold et al. 1994b; 1997b; Williams et al. 1992).

6. Dreams create story lines to explain and integrate all the dream elements in a single confabulatory narrative (Blagrove 1992b; Cipolli & Poli 1992; Cipolli et al. 1998; Foulkes 1985; Hobson 1988b; Hunt 1991; Montangero 1991).

7. Dreams show increased and intensified emotions, especially fear-anxiety (Domhoff 1996; Merritt et al. 1994; Nielsen et al. 1991), which appear to integrate bizarre dream features (Merritt et al. 1994), and may even shape the narrative process (Seligman & Yellin 1987). Although the trend toward a predominance of negative emotion is prominent in most studies, other workers have found more balanced amounts of positive and negative emotion (for a good review, see Schredl & Doll 1998). Emotion also ranks as a prominent explanatory focus in functional theories of dreaming (e.g., Cartwright et al. 1998a; Greenberg et al. 1972; Kramer 1993; Perlis & Nielsen 1993).

8. Dreams show increased incorporation of instinctual programs (especially fight-flight), which also may act as powerful organizers of dream cognition (Hobson 1988b; Hobson & McCarley 1977; Jouvet 1973; 1999).

9. Volitional control is greatly attenuated in dreams (Hartmann 1966b). The dreamer rarely considers the possibility of actually controlling the flow of dream events (Purcell et al. 1986) and, on those infrequent occasions when this does occur, the dreamer can only gain lucidity with its concomitant control of dream events for a few seconds (LaBerge 1990). Unlike the rarer form of dream control offered by lucidity, however, the more mundane self-control of thoughts, feelings and behavior may be fairly common in dreams (Kahan 1994).

All of these features can be found in REM dreams, and most REM dreams contain a majority of these features. Contrastingly, they are found relatively rarely in NREM reports (see Nielsen 1999). This is the empirical basis of our contention that all of these features will eventually be explainable in terms of the distinctive physiology of REM sleep.

We interpret the foregoing evidence as strongly supporting our conclusion that there are clear-cut and major differences among the states of waking, sleeping (NREM) and dreaming (REM) at the phenomenological level. We take the robust evidence for quantitative differences in amount of NREM and REM sleep mentation as convincing proof of the validity of an important role for not only activation (factor A) but for the two other factors, information source (I) and modulation (M) in our AIM model. In addition, we take the evidence that state transitions are gradual rather than discontinuous and the evidence that correlations between phenomenology and physiology are statistical rather than absolute as further support of this model.

2.2. Overview of the NREM-REM sleep mentation controversy

Although the discovery of REM sleep and its strong correlation with dreaming (Aserinsky & Kleitman 1953) initially led to the strong hypothesis that dreaming occurred *only* during REM sleep (Dement & Kleitman 1957b), this hypothesis was clearly refuted by the discovery that reports of dreaming could be elicited from NREM sleep (Foulkes 1962) and that reports of dream-like mentation could also be obtained at sleep onset (Foulkes & Vogel 1965) and even from quiet waking (Foulkes & Fleischer 1975; Foulkes & Scott 1973). Given dreaming's lack of absolute state specificity, some investigators sought the psychophysiological correlates of specific dream features in the phasic events of REM and NREM sleep (Molinari & Foulkes 1969; see Kahn et al. 1997 and Pivik 1991 for reviews). Again, weak but consistently positive quantitative relationships were found (Kahn et al. 1997; Pivik 1991).

This lack of specificity led at least some investigators ultimately to conclude that investigations of REM sleep neurophysiology could provide no data helpful to understanding the genesis of dreaming (e.g., Bosinelli 1995; Foulkes 1990; 1991; 1993b; 1995; 1996a; 1997; Moffitt 1995). Such a view was encouraged by reports suggesting that in fact the differences between REM and NREM mentation were not nearly as great as had first been reported (e.g., Cavallero et al. 1992). In this section, we will present our reasons for rejecting these conclusions (see also Nielsen, target article).

How could the firm conclusions of the pioneer era (1955–1975) have apparently dissolved in the subsequent era of growing controversy (1975–1999)? In this section, we will analyze some of the scientific problems that led to the decline of the sleep-laboratory paradigm as this psy-

chophysiological approach lost much of its initially enthusiastic support. In the subsequent section we will turn our attention to the concomitant development of cellular and molecular neurobiology and show how the findings of basic research provided an alternative approach.

2.2.1. REM sleep dreaming is not qualitatively unique. While dream studies generally agree that REM reports are more frequent, longer, more bizarre, more visual, more animated and more emotional than NREM reports (Table 1), a pair of papers published in 1983 (Antrobus 1983; Foulkes & Schmidt 1983) led some researchers to the remarkable conclusion that the "characteristics [of dreaming] are pretty much the same throughout sleep" (Moffitt 1995) and that "dreaming in other sleep stages is not qualitatively different from REM dreaming" (Foulkes 1995). Because these papers are so central to the REM-NREM dreaming debate, we now offer a detailed review and critique of their findings and interpretations.

At the outset, it is important to point out that neither article actually concluded that REM and NREM dreams are indistinguishable, or even substantially the same, in either their quantitative or their qualitative features. In regard to qualitative features, Antrobus (1983) reported that when judges rated 154 REM and NREM reports for their relative "dreaminess" (using scales based on "visual imagery, bizarreness, hallucinatory quality and storylike quality"), they correctly identified 93% of the reports as either REM or NREM, indicating that REM dream reports were much more dreamlike than NREM reports. Similarly, Foulkes and Schmidt (1983, p. 276) concluded that "REM reports are likely to be significantly more dreamlike qualitatively (e.g., in character density, setting clarity) than typical NREM" reports, even when elicited after only five minutes of stage REM.

In regard to quantitative features, when Foulkes and Schmidt (1983) looked at 160 REM and NREM reports and characterized their lengths by the number of "temporal units" (narrative events), their data showed that temporal sequences (sequential events = temporal units − 1) were 14 times more common in REM reports than in NREM reports. In a similar way, Antrobus analyzed total recall frequency (TRF), which reflects the number of words in a report used to describe sleep mentation, and reported that word count significantly distinguished REM from NREM reports ($F = 95.52$). Using the same reports (J. Antrobus, personal communication), we have determined that the REM reports collected by Antrobus had a median length 6.4 times longer than their matched NREM reports, a number similar to the ratio of 7.0 obtained in a home study using reports from spontaneous awakenings (Stickgold et al. 1994a).

Since both Foulkes and Schmidt (1983) and Antrobus (1983) report such impressive differences between REM and NREM reports, one might wonder how and why these very authors have come to argue so strongly for a phenomenological sameness of these states. The critical question, raised by Foulkes and Schmidt and by Antrobus, pertains to the origin of the differences between REM and NREM reports, "whether there are . . . qualitative . . . differences as well as quantitative ones, and . . . whether such differences are merely attendant upon or are independent of the quantitative ones" (Foulkes & Schmidt 1983, p. 269). Or, as Antrobus wonders, whether "judges of Dreaming [dreaminess] implicitly rely on a dimension similar to the Total Recall Freq." (p. 562). It is this analysis that has led subsequent writers to claim that "when the quantitative characteristics of reports . . . from REM and nonREM . . . sleep are adjusted for length there are no differences in the characteristics of the reports" (Moffitt 1995, p. 19).

The normalization-for-length technique has been subsequently used to argue that bizarreness differences between REM and slow wave sleep (SWS) reports (Colace & Natale 1997), the number of dream-like features in a report (Fein et al. 1985; Rosenlicht & Feinberg 1997), memory sources of dreams (Cavallero et al. 1990) and even dream bizarreness itself (Bonato et al. 1991) are all directly and causally dependent on report length independent of sleep stage. Similar arguments have been advanced to explain correlations between dream bizarreness and creativity (Livingston & Levin 1991).

We will shortly reiterate our introductory arguments against this line of reasoning. Meanwhile, we emphasize some of these authors' own data that favor placing a strategic emphasis on the *differences* between REM and NREM mentation rather than using the similarities as a rationale for rejecting the cognitive neuroscience paradigm in favor of a purely cognitive description of mental states. (A similar critique of purely cognitive descriptions can be found in Nielsen 1999; and his target article.)

For example, Antrobus has recently shown that the REM/NREM distinction exerts a far greater effect on bizarreness than diurnal activation (Antrobus et al. 1995). He attributed the observed increase in bizarreness in REM reports to the increased activation seen in that state (Antrobus et al. 1995). It is also noteworthy that purely visual (versus verbal) imagery gave robust REM/NREM differences suggesting a differential sensory activation between the two states (Antrobus et al. 1995). And even when REM and NREM dreams were adjusted for length (a procedure we will shortly argue to be invalid), both Antrobus (1983) and Foulkes and Schmidt (1983) still found significant differences (e.g., in character density and setting clarity) between the two states. Notably, the persistence of a REM/NREM effect on bizarreness, visual imagery, and several other dream features in spite of normalization for report length has recently been confirmed (Casagrande et al. 1996b; Faucher et al. 1999; Nielsen 1999; and his target article; Raymond et al. 1999; Waterman et al. 1993). For example, when analysis of covariance (with report length as the covariate) is used to partial out the effect of report length on dream features, REM reports were still judged significantly more visual and bizarre than sleep onset or stage 2 reports (Casagrande et al. 1996b) and more visual than NREM reports (Waterman et al. 1993).

Even when dream features appear to be specifically linked to distinctive REM physiology, interpretations can still be cast toward either camp. Hong et al. (1997) reported an impressive correlation between visual imagery and REM density ($r = 0.8$), which we would argue as evidence for a dependence of dream imagery on a qualitative feature of REM sleep. But Antrobus et al. (1995) consider this to be another example of the simple dependence of dream content on levels of brain activation, arguing that rapid eye movements are not under strict brainstem cholinergic control, but come increasingly under the control of the frontal eye fields as general cortical activation increases.

Whatever one's assessment of the similarity versus difference argument, it is clear that none of the analyses in these two papers can distinguish between two competing

hypotheses: (1) that dream features are dependent on report length; and its simpler converse (2) that report length is dependent on dream features. We now consider the arguments in favor of the second hypothesis, which we have adopted in our own work.

2.2.2. The relationship between dream features and dream report length. That report length depends on dream features was first implied by Hunt (1982) in his analysis of dreaming as fundamentally visuospatial versus verbal-propositional and was then explicitly proposed by Hunt et al. (1993). We agree with their logical assumption that reports with more dream features will require more words to describe them. For example, a report with such dream features as self-representation, visual hallucination, emotion, narrative plot, and bizarreness will almost certainly be longer than a report with none of these features. Similarly, it is highly unlikely that a report with a word count of only seven words, the median length of the Antrobus (1983) NREM reports (J. Antrobus, personal communication), could possibly have more than one of the above features.

Inexplicably, Antrobus (1983) and Foulkes and Schmidt (1983) both seem to regard word count and content as independent of each other. In doing so, each has emphasized a very different explanation. Although conceding that alternative explanations were "in no way excluded by these findings," Antrobus (1983) concluded that the NREM reports were shorter due to a defect in "the ability of the subject to recall and describe the [dream] events" (p. 567). In this view, the shorter reports failed to include dream features which were nonetheless present in the NREM dream itself. To us this seems, at best, a risky assumption. In contrast, Foulkes and Schmidt (1983) concluded that the shortened reports and the rarity of dream features reported resulted from differences in dream production. On this view, the differences reflected "the relative paucity and superficiality of mnemonic units active during NREM sleep" (p. 279) compared to REM sleep. The conclusion of Foulkes and Schmidt (1983) is strikingly similar to our position, which is that the relative brevity of NREM reports reflects a decrease in the types (superficiality) and number (paucity) of dream features present in the conscious experience reported in them. If Foulkes really agrees with us on this point, he cannot then also countenance controlling for word count in evaluating reports.

Analyzing the same data set used by Antrobus (1983) we have shown that REM/NREM differences can not be explained simply in terms of report length (Porte & Hobson 1986). Thus we agree with Antrobus when he pointed out that there is still a part of the REM/NREM variance that Dreaming (i.e., judges' idiosyncratic scales for "dreaminess") picks up better than a Total Recall Frequency factor.[1] Similarly, Foulkes and Schmidt (1983) reported that some residual REM/NREM differences in temporal unit composition (e.g., in character density) persist even after report length is controlled. Residual stage differences following normalization for report length in these as well as additional studies have recently been reviewed by Nielsen (1999).

In the face of such unambiguous statements, it is critical to try to understand why these results have been so frequently and so passionately misinterpreted. In part, the erroneous interpretations were encouraged by the original authors. For example, Antrobus (1983, p. 567) concluded that "although there are slight differences . . . it is quite clear that the global judgment of Dreaming adds little, if anything, to Total Recall [Frequency] with respect to the association with the sleep stages REM and NREM." Similarly, Foulkes and Schmidt (1983; p. 279) concluded that "*most* typically observed inter-stage differences in dream reports stem from different lengths rather than the different stages of the reports" (emphasis added). Because they have conflated causality with correlation, both Antrobus and Foulkes and Schmidt unjustifiably assume that most of the differences seen can be explained as correlates of report length. We disagree on the basis of the following studies.

Recent evidence provides strong support for Hunt's proposition that report length reflects the number and intensity of dreamlike features prior to awakening. Hunt et al. (1993) have argued "it is not the length of the dream that somehow makes bizarreness more likely, but . . . it is more parsimonious to conclude that episodes of bizarreness within the dream are one major determinant of overall dream length . . . making length a necessary consequence of bizarreness and not the other way around" (p. 180). In addition, Hunt et al. (1993) note that Hauri et al.'s (1967) factor analysis of dreams found that bizarreness and report length significantly load on the same factor (and therefore strongly co-vary), "which would make their enforced statistical separation highly questionable" (Hunt et al. 1993, p. 181). In other words, if quantity follows quality and is, in fact, caused by it, then longer reports are needed to describe dreamier dreams. On this view, word count is perhaps even a direct measure of dreaminess and might well be taken as such.

To support their position, Hunt et al. (1993) first demonstrated that awake subjects used more words to describe a visually bizarre picture than a mundane picture. They then showed that the bizarreness scores correlated positively with the number of words devoted to describing the bizarre episodes. Finally, they showed that normalizing dream features for report length actually eliminated the correlations of bizarreness with non-verbal imagination test scores. Hunt et al. therefore concluded that bizarreness directly determines a major component of report length and that controlling for total word count introduces an artifactual dilution of bizarreness scores.

In summary, a critical review of the papers of Antrobus (1983) and Foulkes and Schmidt (1983) reveals that these papers report significant quantitative differences in the features of REM and NREM dreams. Both papers also find features such as dreaminess or character density to differ significantly between REM and NREM dreams *even when report length is unjustifiably normalized.* Neither study reports data that argue against the contention that the strong correlation between report length and dream features occurs because reports with more dream features require more words to describe them (Hunt et al. 1993; Nielsen 1999). We urge the collection of additional data to further clarify the nature of these REM/NREM differences. Such data should include ample numbers of reports, collected longitudinally in naturalistic settings, which are obtained from home awakenings physiologically monitored with unintrusive devices such as the Nightcap (e.g., Rowley et al. 1998).

2.3. Methodological considerations in the study of dreaming

The study of mental states is replete with methodological shortcomings and conceptual confusions. We believe that

some of these areas of confusion can be clarified in a manner that could increase consensus. In what follows, we address five methodological issues to point out the nature of the problems, offer clarifications, and suggest possible resolutions.

2.3.1. The reduction of psychological states to narrative reports. The most profound problem in studying conscious states is the necessity of reliance on verbal reports. This method is problematic because these accounts are just *reports,* not the subject's experience of the states themselves. This reduction of conscious experience to prose has at least three important ramifications:

(1) A multimodal conscious experience including pseudosensory perceptual, emotional, and motoric dimensions is reduced to only one mode, that of narration. (To emphasize this point, we merely point out that if a picture is worth a thousand words, we certainly are not getting the whole picture with a seven-word report!)

(2) The narratives describing sleep state mentation are all generated during the waking state and are thus likely to mix, if not contaminate, the dreaming phenomenology with the phenomenology of waking (for a discussion of this point relative to dream meaning, see Hunt 1989, p. 9).

(3) Analysis of narrative dream reports is extremely limited in its power to recreate or model the true underlying mechanism of dream production at any fundamental, primordial level of explanation (be it cognitive-mnemonic, linguistic or neuropsychological) because narratives about experience display a high degree of what Pylyshyn (1989) terms "cognitive penetrability."

Pylyshyn's point can be applied to dreaming as follows. The behavior of the dream production system is highly malleable using the same cognitive processes invoked to explain its behavior such as the dreamer's goals and beliefs (see Pylyshyn 1989). For example, in the case of the dreamer's goals, the frequency of overall dream recall as well as lucidity can be greatly increased by auto-suggestion techniques that employ many of the same cognitive abilities (e.g., imagination and visualization) that most theorists believe contribute to dream production itself (see sect. 3.3). In the case of beliefs, the meaning of a dream experience *while it is occurring* is highly dependent on the dreamer's personal (and changeable) philosophy of what dreaming is (e.g., a message from a deity, a psychopathomimetic experience, "travel outside the body," etc.). According to Pylyshn (1989) such highly penetrable experiences, rather than illustrating primordial cognitive mechanisms, instead reflect "the nature of the representations and . . . cognitive processes operating over these representations" (p. 81), which, in the case of dream reports, is language itself. Given that Pylyshn (1989) asserts that cognitive penetrability can affect even highly objective and replicable psychological data (such as the visualized-image-size/image-scanning-time relationships described by Kosslyn & Koenig 1992), penetrability is all the more likely to influence the highly elaborated and individualistic phenomenon of dream reporting. The rendering of dream reports in conventional (wake state) grammar and syntax may, therefore, tend to obscure important differences between the actual experiences of waking and dreaming.

These considerations raise the concern that using the sentence or the word as a unit for quantifying mental activity may say more about language than about the multimodal nature of conscious experience. This is important because so many researchers consider the quantification of report length as the single most salient feature of a dream. In this context, it is also worth noting that verbal retrospective reports are often considered inadequate to describe mental states that are closer to dreaming than to waking mentation. These states include religious conversion, near-death experience, functional psychosis, delirium, drug-induced conditions, and other altered states of consciousness.

This aspect of the REM physiology-dream mentation controversy may be particularly relevant to the current debate about self-representation and bizarreness in dreams of children aged 3 to 8 (see Foulkes 1990; 1993b; 1996a; 1996b; 1997; Resnick et al. 1994). Based upon an extensive longitudinal study (Foulkes 1982b) and a later cross-sectional study (Foulkes et al. 1990), Foulkes asserted that "dreaming is absent until ages 3 to 5 and does not assume the form of adult dreaming until ages 6 to 7" (Foulkes 1997, p. 4). Foulkes hypothesizes that, lacking or being deficient in their ability to consciously mentally represent their perceptuo-behavioral experience, young children (like animals) may not experience dreaming in spite of having an abundance of REM (Foulkes 1990; 1993c). He argues further that dreaming is "a high-level symbolic skill, a form of intelligent behavior with cognitive prerequisites and showing systematic development over time" (Foulkes 1993c, p. 120), and that dreaming has, as its prerequisite, conscious representational competence (Foulkes 1990; Foulkes et al. 1990). As evidence to support this, he cites studies in which he finds very low recall of dreaming and little bizarreness prior to age 5 (Foulkes 1982b; Foulkes et al. 1979), low rates of reporting at ages 5–8 (Foulkes 1982b; Foulkes et al. 1990), acquisition of kinetic versus static imagery only after age 6 (Foulkes et al. 1990), and acquisition of self-representation as an active dream participant as well as narrative continuity only after age 7 (Foulkes et al. 1990; 1991). Further, from his data showing correlation of report rate with measures of visuospatial versus verbal skills (Foulkes et al. 1990), Foulkes (1993b) suggests that "young children may fail to report dreams because they are not having them, rather than because they have forgotten them or are unable to verbalize their contents" (p. 201). For a recent review see Foulkes (1999).

Subsequent studies have shown that dream bizarreness does indeed increase over ages 3 to 8 (Colace et al. 1993; 1997; Colace & Tuci 1996; Resnick et al. 1994). However, other of Foulkes's findings have not been supported. For example, dream reporting rates in 4- to 5-year olds has been reported to be almost identical to that in 8- to 10-year olds (Resnick et al. 1994). In addition, active self representation in dreams of 4- to 5-year olds has been reported to occur in over 80% of their dream reports (Colace et al. 1995; Resnick et al. 1994). Finally, substantial occurrence rates for bizarre elements have been reported in the dreams of both 4- to 5-year olds (0.45 per 100 words) and 8- to 10-year olds (0.71 per 100 words) (Resnick et al. 1994).

Moreover, although rates of adult dream recall have been related to performance on tests of visuospatial skill (Butler & Watson 1985), rates of dream recall have also been correlated with individual differences in visual memory (Schredl et al. 1995). Therefore, any ontogenetic changes in visual memory would confound the effects of developmental changes in higher order visuospatial skills on dream reporting rates in children.

Overarching these conflicting data, however, is the theoretical point bearing on the current discussion: that is, that

dream reports are given in waking and thus, of necessity, must be constrained by an organism's waking cognitive and linguistic abilities. At one extreme, it must be conceded that even if a cat had the most vivid of "dreams," it would not be able to report it. Similarly, if a toddler is variously unable (or unwilling) to conceive and verbalize a complex perceptual-emotional-motor REM experience, it does not mean it was not originally experienced in some form which, later in life, might be reported as a dream. In other words, we challenge here the assumption by Foulkes (e.g., 1990) and others (e.g., Bosinelli 1995) that "dreaming" is an experience that can occur only if it can be later reported by an organism possessing linguistic abilities. We recognize that verification of oneiric activity in organisms that are unable to report (or even, possibly, reflect upon) their experiences is currently impossible, although we do not rule out the possibility that new methods may someday provide hints as to the conscious experiences of nonverbal beings (e.g., see Marten & Psarakos 1995).

Nevertheless, as with many other psychological constructs such as emotional expression (e.g., Darwin 1873) or behavioral inhibition (e.g., Goldman-Rakic 1986), such inferences drawn between human developmental as well as mammalian phylogenetic levels has a long scientific tradition. It is, therefore, not inherently invalid to cautiously speculate from adult human oneiric experience to observed REM behavior in infants and animals, especially given the abundant behavioral correlates (e.g., ethologically meaningful oneiric behavior; for a full discussion see Jouvet 1999). Similarly, we specifically suggest that the human neonate, spending as it does more than 50% of its time in REM sleep (Hobson 1989), is having indescribable but nevertheless real oneiric experiences. An infant's waking experience remains essentially indescribable and speculative to us older persons but we do not doubt that infants enjoy some sort of waking conscious experience. For us, it is not at all difficult to imagine that an infant might be experiencing hallucinosis, emotions, and fictive kinesthetic sensations during REM sleep.

Given these caveats, we suggest that more effort be put into the development and use of other methodologies and scales such as the photo-response visual brightness and clarity scale (Antrobus et al. 1987; 1995; Rechtschaffen & Buchignani 1992), temporal unit analysis (Cavallero et al. 1990; Foulkes & Schmidt 1983), computerized content analyses (Gottschalk 1999), the analysis of dream drawings (Hobson 1988b), or the use of affirmative probes (e.g., Herman 1992; Merritt et al. 1994; Pace-Schott et al. 1997a; Stickgold et al. 1997a; see Herman 1992 and Hobson & Stickgold 1994a for further discussion). In other words, we need recourse to more diverse means to elicit detailed descriptions of salient aspects of conscious experience.

2.3.2. The sleep laboratory environment. The sleep laboratory itself constitutes a second major methodological problem. Anyone who has ever slept in a sleep laboratory (as all of us have!) knows that it is an inhospitable and unnatural setting that makes sleep more difficult and less deep than is possible in more naturalistic settings. To appreciate this point, the reader need only imagine going to an unfamiliar place in an inner city neighborhood of dubious safety, encountering a technician who is a stranger and often of the opposite sex, having ten electrodes affixed to the scalp with cement that smells like airplane dope and then being bid "goodnight" and "pleasant dreams." Hence the famous first night effect (objectively poor sleep owing to discomfort and anxiety) often extends to a second night, and may contribute to a constriction of dream experience (as in dreams of the sleep lab setting) over even longer times. The laboratory environment may even alter the content of dreams recalled from spontaneous awakenings in the laboratory at the end of a night's sleep as evidenced by the high frequency of laboratory references in morning spontaneous awakening REM and NREM laboratory dream reports (Cicogna et al. 1998).

Studies such as those of Dement et al. (1965), Domhoff and Kamiya (1964), Okuma et al. (1975) and Whitman et al. (1962) have shown substantial incorporation of the experimental situation into laboratory dream reports particularly on the first night in the laboratory but persisting, at a lower level, into subsequent laboratory nights (Dement et al. 1965; Domhoff & Kamiya 1964). Similarly, content differences have been noted between laboratory and home dreaming (Domhoff & Kamiya 1964; Domhoff & Schneider 1999; Hall & Van de Castle 1966), although it has been argued that these differences are very small (Domhoff & Schneider 1999). Although these early studies were confounded by spontaneous (home) versus instrumental (laboratory) awakening conditions (as has been noted by Foulkes 1979), later studies controlling for reporting conditions (Lloyd & Cartwright 1991; Weisz & Foulkes 1970) still found some content differences between the home and laboratory dreams of adults. Waterman et al. (1993) emphasize that home-laboratory differences can arise from both environmental factors and factors related to investigator expectancies and, therefore, both should be controlled. In our view, full adaptation to the sleep lab may take four days or longer (see Domhoff & Kamiya 1964) exceeding the length of most laboratory studies.

As in the case of NREM compared to REM dreaming, we are not arguing for a gross, qualitative distinction between home and laboratory dreams. Laboratory dreams are, undoubtedly, largely representative of many of the formal and content features of dreaming in naturalistic settings. Nevertheless, we suggest that quantitative constraints on the dreaming experience may be imposed by the laboratory setting so that the full potential expression of certain dream features is limited. Of additional concern is the finding by Antrobus et al. (1991) that REM-NREM differences in both word count and global judgment of dreamlike quality diminish over 14 nights in the sleep laboratory, an effect they attribute largely to motivational factors in dream reporting. Minimizing any such "laboratory-fatigue" confound constitutes further argument for longitudinal awakenings to be performed in the more comfortable environs of the home.

To overcome these problems, several options are possible. First, laboratory studies can simply be extended in time, perhaps recording each subject for a full week. This has obvious disadvantages including inconvenience, high cost, and the above noted motivational effects. A second option is to continue to run relatively short (1–4 night) paradigms, and accept the suppressive effects on sleep architecture and dream content. While perhaps no longer normatively valid, the data obtained would still be at least reliable. A third option, and the one that we have chosen, is to move recording into the home for extended longitudinal studies using the Nightcap (Ajilore et al. 1995; Mamelak & Hobson 1989b; Pace-Schott et al. 1994; Rowley et al. 1998; Stickgold et al. 1994a; 1998b).

2.3.3. The question of "similarity" and "difference." We have long thought that the argument over whether mentation in two states like REM and NREM sleep is more similar or different was specious. Thinking the dilemma to be false, we have ignored or minimized it in our previous writings. However, we now feel obliged to clarify for the reader how the debate over REM and NREM mentation has become inextricably entangled with the larger and more general question of the mind-brain problem. In doing so, we hope to elevate the debate from the parochial to the general level and to make our own position on mind-brain issues crystal clear.

In some ways, understanding the conflicting opinions that swirl around the sleep and dream mental content debate is relatively straightforward. One group of psychologists, exemplified by David Foulkes and the late Alan Moffitt, hypothesizes that the brain and the mind are so loosely linked that the study of the mind need not be constrained – or even informed – by the study of the brain (e.g., Bosinelli 1995; Foulkes 1991; 1993b; 1996a; 1997; Moffitt 1995). This group interprets the empirical data as indicating that mental content does not differ qualitatively across brain states. There is only one dream mentation production system that is more or less active during waking and sleep. In such theories, termed "One-Generator" models of sleep mentation by Nielsen (1999), it is only the fluctuating level of cognitive activation that determines differences between REM and NREM sleep in report length as well as in the broad range of dream features that co-vary with report length. By taking this position, these psychologists minimize the importance of physiology, which they assert to be irrelevant to the understanding of dreaming. How cognitive activation could be independent of brain activation is a question not addressed by these scientists.

Another group, consisting largely of psychophysiologists, holds that the mind and the brain form an integrated system, so tightly linked within and across states that detailed qualitative and quantitative distinctions at either level of analysis imply the existence of isomorphic distinctions at the other. This is the position that we take. For us, the cognition production system *is* the brain. And, of course, it is always the *same* brain. But we know that the brain's mode of information processing changes radically across states. So, therefore, must its mental products. Nielsen (1999) terms this point of view a "Two-Generator" model of sleep mentation. For us, the state-specific changes in brain function virtually guarantee concomitant changes in mental function, even if our psychological methodology may still be inadequate to identify these changes (just as for many years the physiological changes also eluded us!).

With respect, we suggest that the failure to demonstrate psychological differences concomitant with physiological ones must be laid at the door of inadequate psychological methodology. If psychology has so far failed to document the robust phenomenological differences between waking and dreaming that most people experience every day of their lives, then more vigorous and more creative psychological research is needed. Otherwise we are faced with the absurd and unacceptable conclusion that brain and mind have nothing to do with each other.

That even a single, "One-Generator" system (i.e., a "dream mentation production system") may show dramatically different features in different states is in no way a self-contradiction. To our way of thinking, states of the brain are analogous to other dynamic states of matter. Consider, for example, the way that liquid water changes state with changes in temperature: above 100° C it is steam; below 0° C it is ice. These states are analogous to the states of waking, NREM sleep, and REM sleep in the brain (as well as to less common mental states such as coma, hypnosis, and mania). No one would say that in the frozen state (ice) or in the vapor state (steam) that the material is not still water. Nor could any sentient person ignore the obvious differences in the properties and behavior of water across states. We believe that it is equally inappropriate to argue that since there is a single dream production system (i.e., the brain-mind), that the properties and behavior of its products, for example, dreams, must be identical or even similar across different states. Such an important error in scientific thinking would lead to minimizing or missing entirely the change in matter (in this case the brain) that underlies the change in its state-dependent properties (in this case, consciousness).

The question of whether REM and NREM mentation are the same or different has often devolved into a search for characteristics of mentation that are absolutely unique to REM sleep. We consider this quest to be a fool's errand and indeed no absolute qualitative distinction between the two states has yet been documented. Since the late 1950s, many sleep laboratory studies have shown substantial recall of mentation from NREM, thereby obviating an exclusive association of sleep mentation with REM (Cicogna et al. 1998; Foulkes 1962; 1966; Foulkes & Rechtschaffen 1964; Goodenough et al. 1959; 1965b; Kamiya 1961; Molinari & Foulkes 1969; Pivik & Foulkes 1968; Rechtschaffen et al. 1963; Salzarulo & Cipolli 1979; Stoyva 1965; Zimmerman 1970; see Foulkes 1967, Herman et al. 1978, and Nielsen 1999 for reviews). For example, among nine studies, the percentage of NREM awakenings yielding at least minimal recall varied from 23 to 74% (Foulkes 1967) and, as noted, Nielsen (1999) has found an average NREM recall rate of 42.5% over 33 published studies. Recall rates similar to those of NREM in general have even been obtained from stages III and IV of NREM (e.g., Bosinelli 1995; Cavallero et al. 1992; Goodenough et al. 1965b; Herman et al. 1978; Nielsen 1999; Pivik & Foulkes 1968; Salzarulo & Cipolli 1979; Tracy & Tracy 1974). In a review of eight studies of stages III and IV mentation, Nielsen (1999) found an average recall rate of 52.5 (+18.6)%, but also notes that a substantial percentage of subjects never recall stage III and IV mentation or require several nights of awakenings before reporting such mentation.

The findings of several studies have countered the hypothesis that NREM mentation is simply recall from previous REM (Foulkes 1962; 1967; Foulkes & Rechtschaffen 1964; Goodenough et al. 1965b; Rechtschaffen et al. 1963), although report length does drop precipitously following the end of REM periods (Stickgold et al. 1994a).

The fact that differences are *not absolute* does not mean however that *no* differences exist. Indeed, all the evidence shows that such differences *do* exist and we have already advanced good reasons to believe that these may have been seriously underestimated. For example, similarities in dream features such as bizarreness may be inflated when report length is controlled in REM and NREM reports (Hunt et al. 1993) and REM-NREM bizarreness differences may persist even when report length is partialled out (Casagrande et al. 1996b; Nielsen 1999; Waterman et al. 1993). In addition, recent work comparing sleep onset REM and NREM dreams using an experimental protocol which controlled for previ-

ous sleep and waking time has shown that sleep onset REM periods are specifically related to physiological signs of REM whereas NREM dreams were related to intrusions of waking into NREM (Takeuchi et al. 1999b). These authors conclude that the mechanisms underlying REM and NREM dreaming must, therefore, differ (Takeuchi et al. 1999b). We thus conclude that while *some* NREM dreams approach REM dreams in length, vividness, dreaminess, and bizarreness (Cicogna et al. 1998; Foulkes & Schmidt 1983; Herman et al. 1978; Nielsen 1999) and while "dreamlike" versus "thought-like" mentation may predominate in some NREM reports (Foulkes 1962; Nielsen 1999; Rechtschaffen et al. 1963; Zimmerman 1970), NREM reports are far more likely than REM reports to be short, dull, and undreamlike (Nielsen 1999; Rechtschaffen et al. 1963).

Many of the above-noted problems inherent in assessing the similarity versus difference of two phenomena can be addressed with improved methodologies. For example, when two states (such as REM and NREM) are being compared in terms of specific parameters (such as bizarreness) to a third state (such as waking), the question of the similarity versus difference between the two states becomes much more tractable.

2.3.4. The source and fate of dream memory. A tendency to emphasize psychological similarity has also characterized recent studies on the memory sources of REM and NREM dreams. Using a modification of Tulving and Thomson's (1973) classification of memory sources and an experimental free association technique, Cavallero and his colleagues initially found a distinct difference in memory sources between early-night REM and NREM mentation (Bosinelli 1991; Cavallero & Cicogna 1993; Cicogna et al. 1986). Early-night NREM sources consisted primarily of discrete biographical episodes while REM sources were a mixture of episodic, abstract self-referential and semantic sources (Bosinelli 1991; Cavallero & Cicogna 1993; Cicogna et al. 1986). This observation fits with the commonly accepted distinction between NREM dreaming as a simpler and REM dreaming as a more complex state of consciousness.

However, when REM and NREM reports were collected later in the night and matched for "temporal unit composition" (a procedure akin to diluting bizarreness by controlling for word count), the same researchers emphasized the similarity of memory sources between REM and NREM (Bosinelli 1991; Cavallero & Cicogna 1993; Cavallero et al. 1988; 1990; 1992; Cicogna et al. 1991; Fagioli et al. 1989). Likewise, Cicogna et al. (1991) reported few REM/Stage 2 differences in number of temporal units, implausibility, self presence, settings or characters. Nonetheless, as in the case of dream content (Antrobus 1983; Foulkes & Schmidt 1983), some residual state-related memory source differences continued to be reported (Cavallero & Cicogna 1993; Cavallero et al. 1990; 1992; Cicogna et al. 1991) and these need to be explained.

The research on memory sources for mentation among the different behavioral states overlooks the far more robust difference in the overall functioning of memory processes that distinguishes sleep from waking. This is the notorious difficulty of recalling dreams or any other mental content following either instrumental laboratory or spontaneous awakening. Many dreamers are aware that recall actively eludes them as they awaken. And even when dream recall is confident and detailed, it is common for subjects to assert that they are sure that there was much more antecedent dreaming that could not be recalled. One reason for the neglect of this robust phenomenon is that it is difficult to study something, in this case memory, that isn't there! But the very absence of recall is a datum which any dream theory must explain, especially in the face of the robust brain activation in REM sleep!

Freud's famous explanation was that dream forgetting was an active function of repression. We have instead attributed this prominent failure of recall to a state dependent amnesia caused by aminergic demodulation of the sleeping brain (Hobson 1988b). The waking level of aminergic modulation falls to 50% in NREM sleep and to nearly zero in REM (Hobson & Steriade 1986; Steriade & McCarley 1990a). It would appear that the intense activation of REM must overcome this demodulation and persist into subsequent waking in order for very vivid dreams to be remembered. In our view, the low level of production and recall of NREM mentation is due to the additive effects of inactivation and demodulation.

This hypothesis is consonant with subjective experience. For example, when one introspectively compares recall of a night's dreaming with that of a corresponding waking epoch, one of the most obvious differences lies in the far greater amount of detail that can be recalled in waking. Moreover, it is commonplace for long dreams to have complete scene shifts of which the dreamer takes no significant cognitive account. If such orientational translocations occurred in waking, memory would immediately note the discontinuity and seek an explanation for it. This intuitively convincing difference between memory for dreaming and memory of waking mentation is confirmed by several empirical studies (see below).

Although the frequent inability to recall dreamed experience in subsequent waking has been a robust finding in dream research (Goodenough 1991), there is also strong evidence of deficient memory for prior waking experience in subsequent sleep. For example, little continuity has been shown between pre-sleep stimuli and the content of REM dreaming when this phenomenon has been probed using the following paradigms:

1. Specific experimental pre-sleep stimuli in the form of films have little effect on dream content (Cartwright et al. 1969; DeKoninck & Koulack 1975; Foulkes et al. 1967; Foulkes & Rechtschaffen 1964; Goodenough et al. 1975; Karacan et al. 1966; Witkin 1969; Witkin & Lewis 1967).
2. Specific experimental pre-sleep stimuli such as static visual images or altered social milieu are rarely incorporated into dreams (Carpenter 1987; Orr et al. 1968; Shevrin & Fisher 1967).
3. Specific pre-sleep waking behavioral or thought experiences are not easily detectable in subsequent dreams (Bakeland 1971; Bakeland et al. 1968; Breger et al. 1971; Cartwright 1974b; Hauri 1970).
4. Presleep mentation is infrequently picked up by the dream process (Rados & Cartwright 1982; Roussy et al. 1996; 1997).
5. Naturalistic daytime events rarely enter dream content, casting grave doubt on the classical psychoanalytic concept of day residue as dream instigator (Epstein 1985; Harlow & Roll 1992).
6. Pre-sleep modification of biological drives or perceptual experience has very weak effects on dreaming (Baldridge et al. 1965; Bokert 1968; Dement & Wolpert 1958;

Roffwarg et al. 1978). (For reviews see Arkin & Antrobus 1978 and Cavallero & Cicogna 1993.)

It must, therefore, be concluded that because dreaming is so little shaped by pre-sleep experience, memory systems active during REM sleep have extremely poor access to recent waking memories. Even if dreaming is concerned far more with emotionally salient content than with current events, it is remarkable that the dream construction process fails to incorporate recent episodic memories, including emotionally salient ones, to any significant extent. Two experimental exceptions to this generality, however, should be noted. The first involves the practice of dream incubation whereby focused pre-sleep attention on a specific concern has been shown to increase its rate of occurrence in subsequent dreaming (Saredi et al. 1997). Dream incubation techniques, however, introduce substantial confounds in the form of artificially imposed practice effects as well as the focus on emotionally salient issues. The second involves the finding by Rosenblatt et al. (1992) that significantly more of cartoon segments viewed prior to sleep were recalled following REM versus Stage 2 NREM awakenings, a difference which disappears if a 30 second pre-reporting waking delay is interposed after awakening. Following the arousal-retrieval model of Goodenough (1991), Rosenblatt et al. attribute this REM-NREM difference to greater mnemonic capacity immediately following post-REM versus post-NREM awakenings resulting from greater immediately pre-awakening cortical arousal in REM versus NREM. Using the semantic priming task, we have recently reported a similarly positive mnemonic effect of pre-awakening REM versus NREM for associative memory processes (Stickgold et al. 1999b). Certain forms of memory, such as generating associations to weakly related word primes, may, in fact, be preferentially enhanced by both the activation and the neuromodulatory differences (see sect. 4) between REM and NREM (Stickgold et al. 1999b). In contrast, greater sleep inertia (Dinges 1990) following NREM awakenings (a phenomenon undoubtedly reflecting low pre-awakening brain activation) may less selectively impair a wide spectrum of mnemonic processes.

Even within sleep, memory appears impaired. If episodic experiences within sleep were to persist in the sleeper's memory, one would expect greater content and thematic continuity between contiguous REM periods than more distant REM periods. But despite the fact that content and thematic continuity of successive dreams is greater within the same night than across nights, continuity does not differ between contiguous and noncontiguous REM periods of the same night (Cipolli et al. 1987; Fagioli et al. 1989).

We have recently completed three preliminary studies that seek to quantify aspects of memory within sleep and to compare sleep memory to waking memory. In the first study, 27 subjects became aware of and could later recall three aspects of their memory functioning (semantic, recent, and remote episodic) more often during two waking experiences than during dreaming. Since both types of waking experience sampled were much shorter than the duration of a night's dreaming, results further support the concept of a mnemonic deficiency in dreaming compared to waking (Pace-Schott et al. 1997a).

A second study examined perceived duration of dreaming. The 22.5 minute median perceived duration of dreams by 54 subjects was associated with an unexpectedly large variation. Even ignoring the highest and lowest 10% still left a 24-fold variation. Such wide variance in a basic memory function further suggests a profound alteration of memory processes in dreaming as compared to waking (Stickgold et al. 1997a).

In the third study, 11 subjects recorded the processes by which a total of 103 dreams were recalled. Fifty-two reports (50%) were recalled in "chunks" (i.e., entire dream segments were recalled as units). Another 38 reports (37%) were recalled all at once upon waking and 13 reports (13%) were recalled gradually. Nine of the 11 subjects reported at least one dream recalled in chunks, and there were often significant delays between the recall of different "chunks." These results point strongly to the presence of stored dream memories which cannot be readily accessed on awakening and further suggests both qualitative and quantitative alterations in basic memory processes during and after dreaming (Stickgold 1998; Stickgold et al. 1997a).

All of the above findings can be regarded as being caused by the failure of recent episodic memory (as defined by Tulving 1994) in sleep. And as we have noted, recent episodic memory is weak across wake-sleep and sleep-wake transitions as well as within sleep itself (Pace-Schott et al. 1997b). We believe that a deficiency of memory in dreaming may go a long way toward explaining such distinctive and robust dream phenomena as orientational instability, loss of self-reflective awareness, and failure of directed thought and attention.

2.3.5. Type I versus Type II statistical analyses. In analyzing studies of dream mentation, it is important to understand the nature of the statistical tests employed. In general, such tests calculate the probability that a specific null hypothesis – normally that there is no difference between two population samples – is or is not true. The most common statistical tests, that is, Student's t-test and ANOVA, measure Type I error, which determines the probability that the obtained results could be explained by the null hypothesis. When the probability is sufficiently low, normally less than 0.05, the null hypothesis is rejected and one concludes that the populations are different. Such analyses, however, provide no information on whether or not the null hypothesis is true. Thus, while a low p-value provides strong evidence that the null hypothesis is false, a high p-value does not necessarily indicate that it is true.

This is relevant to the conclusion of both of the papers we critiqued above. Antrobus (1983) concluded that "the global judgment of Dreaming adds little, if anything, to Total Recall Content with respect to the association with the sleep stages REM and NREM" (p. 567), although his statistics did confirm a significant contribution ($F(1,71) = 15.9$, $p < 0.01$). Nevertheless, this conclusion formed the basis of the wider interpretation that the differences between REM and NREM reports are merely a consequence of enhanced recall in REM.

In the second paper critiqued, Foulkes and Schmidt (1983) concluded that global discontinuity "is stage-invariant [and] *never* significantly discriminated reports from different stages of sleep, even in length-uncontrolled comparisons" (p. 277). Although this was true, it was also true that sleep onset reports contained 2.3 times more global discontinuity than NREM reports, a ratio that increased to more than 3 to 1 when normalized for report length (measured in "temporal units"), a fact that could lead to a conclusion quite different from the one drawn by the authors.

It thus appears premature to conclude, based on these early studies, that robust differences between REM and NREM sleep mentation do not exist. Until studies are carried out that measure Type II error and determine the likelihood that the null hypothesis is correct, it is only safe to say that these studies have failed to demonstrate either the presence or absence of differences between REM and NREM mentation. Under the circumstances, more recent studies reporting the presence of significant differences would appear more easily interpreted.

2.3.6. The need for new approaches. The conclusion that we draw from all these studies is that there are significant differences between the formal aspects of the states of consciousness associated with waking, NREM, and REM sleep. These differences, which are quantitative not qualitative, have not yet been adequately characterized for a variety of methodological reasons. Instead of continuing to argue over this issue, we urge our colleagues to join us in a more creative attempt to capture and measure the dimensions of conscious experience.

Basing the attempt to characterize dreaming solely on verbal reports of the poorly recalled subjective experience of subjects sleeping in unfamiliar, non-natural settings has led, not surprisingly, to a sterile and nonproductive controversy about whether the conscious correlates of waking, NREM sleep, and REM sleep are more similar or different, and to a very unfortunate split in what was once a unified field.

This mind-brain split is akin to the gulf that opened between psychiatry and neurology after Sigmund Freud abandoned the goals of his brain-based Project for a Scientific Psychology and declared brain science off limits to his psychology. To reunify two approaches that belong together, we call for a new neuropsychology of conscious states that integrates from the level of cellular-molecular events to the formal features of the mental states of which they form the substrate.

3. The cognitive neuroscience of waking, sleeping, and dreaming

We now turn our attention to the shifts in activation level, input-output gating processes, and the neuromodulatory balance of the brain that underlie the ultradian REM/NREM cycle in humans and in animals. We first enumerate the profound physiological differences that distinctively differentiate waking, NREM, and REM sleep and show that these differences are as robust as those shown above in the phenomenology of waking, sleeping, and dreaming. Then, we point out relationships between the physiological and phenomenological changes seen as the brain-mind shifts from one state to another, as a prelude to integrative modeling. Our overarching hypothesis is that for each phenomenological difference seen between conscious states it is possible to identify a specific physiological counterpart. The end result is a first approximation of a cognitive neuroscience of brain-mind states.

3.1. Recent findings in human neurobiology

3.1.1. Neuroimaging studies. The experimental study of human REM sleep dreaming has until recently been limited on the physiological side by the poor resolving power of the EEG. Even expensive and cumbersome evoked potential and computer averaging approaches have not helped us to analyze and compare REM sleep physiology with that of waking in an effective way. This limitation has probably helped reinforce the erroneous idea that the brain activation of REM sleep and waking are identical or at least, very similar. However, recent technological advances in the field of human brain imaging have made it possible to document a highly selective regional activation pattern of the brain in REM sleep (Braun et al. 1997; 1998; Maquet et al. 1996; Nofzinger et al. 1997). At the same time, experiments of nature – in the form of strokes – have allowed a correlation of the locale of brain lesions with deficits or accentuations of dream experience in patients (Doricchi & Violani 1992; Solms 1997a).

Before discussing these intriguing new results, it is important to stress the methodological limitations of both the brain lesion and imaging techniques. We know from our long and relevant experience in basic sleep research that neither method can capture many significant mechanistic and functional details that emerge from cellular and molecular level neurophysiology (see Hobson et al. 1986 and Steriade & Hobson 1976 for a full discussion of these issues). For example, it is now clear that the lesion method, applied to the pontine brain stem, gave misleading results regarding both the general role of that region in state control and failed even to hint at the specific functions of its subcomponent nuclei. This is because the lesion method cannot discriminate between the effects of destruction and disconnection and cannot target specific neuronal groups in heterogeneous regions like the brain stem.

It is important to note that the preliminary regional functional neuroimaging studies that we review below suffer from such unavoidable limitations of new technologies as the following (see Rauch & Renshaw 1995 for a more complete discussion). First, one must consider whether or not more efficient functioning of an area might result in less versus more observed metabolism or whether glucose or oxygen uptake by inhibitory interneurons may produce local maxima in areas that are, in fact, less active due to inhibition. Second, there are statistical problems inherent in the small sample sizes used in some of these sleep studies (e.g., Braun et al. 1998; Nofzinger et al. 1997) as well as the repeated comparisons employed by the statistical parametric mapping technique (Friston et al. 1991), which is used by all these investigators. Third, global activation measures like electroencephalographic voltage averaging or cerebral blood flow cannot be expected to reveal mechanistic and functional details because they cannot identify small but influential neuronal populations like the locus coeruleus, the raphe nuclei and the pedunculopontine tegmental nucleus. Fourth, there is the potential of altered sleep physiology due to the sleep deprivation (Maquet et al. 1996) or REM deprivation (Braun et al. 1997; 1998) procedures used to maximize sleep stability and stimulate REM in these studies. And fifth, the functional activity of a brain area may vary with changes in its inputs as most dramatically illustrated by neuroplasticity involving recruitment of dedicated brain areas to subserve new modalities such as the visual cortex in Braille learning (e.g., Pascual-Leone 1999) or the reorganization of visual association cortex following V1 damage (e.g., Baeseler et al. 1999). Additionally, it is possible that normal functional disconnections, as occurs between V1 and visual association cortices in REM (Braun et al. 1998), result in the same neural structures performing differing, state-specific functional tasks.

In spite of these caveats, the widespread use of this tech-

nology and the broad agreement of the data with clinical neuropsychological findings argues strongly for the basic validity of neuroimaging as a tool in cognitive neuroscience (Cabeza & Nyberg 1997; 2000). Specifically in response to the fifth caveat above, strong suggestion that the functions of specific brain areas are similar between REM and wake is provided by the observable enactment of experienced dream movement in the REM sleep behavior disorder (Schenck et al. 1993). Moreover, wake-like function of regional brain areas is preserved in many abnormal states such as focal motor activity during seizures (Adams et al. 1997) or the recruitment of visual association cortex during visual hallucinations (Ffytche et al. 1998; Silbersweig et al. 1995). In future sleep research, many of these limitations may be overcome by the finer temporal and spatial resolution offered by functional MRI (fMRI) imaging (e.g., Ellis et al. 1999; Huang-Hellinger et al. 1995; Ives et al. 1997; Sutton et al. 1996; 1997; 1998; Lovblad et al 1999).

Our review of this new literature is undertaken with these shortcomings in mind. Three factors weighed heavily in our evaluation of these data: (1) their novelty and uniqueness in beginning to describe the role of forebrain subsystems; (2) the surprising concordance in the neuroimaging results that emerged from studies carried out simultaneously by three independent groups; and (3) the complementarity between the lesion and imaging studies that confer the value of a double dissociation on the validity of the inferences drawn.

3.1.2. PET studies indicating regional activation differences between REM sleep and waking. Two very recent and entirely independent PET studies confirm the importance of the pontine brain stem in REM sleep brain activation (Braun et al. 1997; Maquet et al. 1996). This is an important advance because it validates, for the first time, the experimental animal data on the critical and specific role of the pontine brain stem in REM sleep generation. At the same time, these new studies also provide important new data for our understanding of dream synthesis by the forebrain. Instead of the global, regionally nonspecific picture of forebrain activation that has been suggested by EEG studies, all of these new imaging studies indicate a preferential activation of limbic and paralimbic regions of the forebrain in REM compared to waking (Braun et al. 1997; 1998; Maquet et al. 1996; Nofzinger et al. 1997). One implication of these discoveries is that dream emotion may be a primary shaper of dream plots rather than playing a secondary role in dream plot instigation.

3.1.2.1. The PET imaging findings of the Maquet group. Maquet et al. (1996) used an $H_2{}^{15}O$ positron source to study REM sleep activation in their subjects who were then awakened for the solicitation of dream reports. In addition to the pontine tegmentum, significant activation was seen in both amygdalae and the anterior cingulate cortex (Table 2). Significantly, despite the general deactivation in much of the parietal cortex, Maquet et al. (1996) reported activation of the right inferior parietal lobe (Bredman area 40) – a brain region thought to be important for spatial imagery construction, an important aspect of dream cognition. The authors interpreted their data in terms of the selective processing, in REM, of emotionally influenced memories (see also Braun et al. 1997; Maquet & Franck 1997).

3.1.2.2. The PET imaging findings of the Braun group. In another $H_2{}^{15}0$ PET study, Braun et al. (1997) largely replicated the Maquet group's findings of a consistent REM-related brainstem, limbic, and paralimbic activation. In REM compared *individually* to delta NREM and to pre- and post-sleep waking (see Table 2), these authors showed relative activation of the pons, midbrain, anterior hypothalamus, hippocampus, caudate, and medial prefrontal, caudal orbital, anterior cingulate, parahippocampal, and inferior temporal cortices (Braun et al. 1997). Based on their observations, the Braun group then offered the following speculations which are relevant to the neurology of dreaming:

(1) Ascending reticular activation during REM as compared to waking may favor a more ventral cholinergic route leading from the brainstem to the basal forebrain over a more dorsal route via the thalamus.

(2) Activation of the cerebellar vermis in REM may reflect input to this structure from the brainstem vestibular nuclei. We note that these nuclei also constitute an important potential source of neuronal activation causing the unique vestibular features of fictive movement in dreams (Hobson et al. 1998c; Leslie & Ogilvie 1996; Sauvageau et al. 1998).

(3) Noting both a particularly strong REM sleep-related activation of the basal ganglia and the known connectivity of these subcortical structures, Braun et al. suggest that the basal ganglia may play an important role in an ascending thalamocortical activation network. They suggest that this network extends successively from the brainstem to the intralaminar thalamic nuclei, then to the basal ganglia, and back to the ventral anterior and ventromedial thalamic nuclei, and thence to the cortex.

This network contains multiple regulatory back projections including interconnections between the pedunculopontine tegmentum and the striatum further suggesting a possible role for the basal ganglia in the rostral transmission of PGO waves and the modulation of REM sleep phenomena. The extensive interconnections of the basal ganglia and the pedunculopontine area have recently been reviewed by Rye (1997) and Inglis and Winn (1995). The role of the basal ganglia in the initiation of motor activity may, in turn, be related to the ubiquity of motion in dreams (Hobson 1988b; Porte & Hobson 1996).

(4) The REM-associated increase in activation of unimodal associative visual (Brodmann areas 19 and 37) and auditory (Brodmann area 22) cortices contrasted with the maintained (NREM and REM) sleep-related deactivation of heteromodal association areas in the frontal and parietal cortex. Combined with findings of striate cortex deactivation in REM, this group (Braun et al. 1998) has subsequently theorized that, during REM, internal information is being processed between extrastriate and limbic cortices while they are functionally isolated from the external world both in terms of input (from the striate cortex) and output (via the frontal cortex).

(5) The prominent decrease in the executive portions of the frontal cortex (dorsolateral and orbital prefrontal cortices) contrasts with the REM-associated increase in activation of the limbic associated medial prefrontal area. This medial area region has the most abundant limbic connections in the prefrontal cortex, has been associated with arousal and attention, and disruption of this area has been shown to cause confabulatory syndromes formally similar to dreaming. (Note also the dream-wake confusional syndrome associated with anterior limbic cortical lesions reported by Solms 1997a.)

3.1.2.3. The PET imaging findings of the Nofzinger group. Also confirming widespread limbic activation in REM

sleep, Nofzinger et al. (1997) described increased glucose utilization in the lateral hypothalamic area and the amygdaloid complex using an 18F-fluoro-deoxyglucose (FDG) PET technique (Table 2). The largest area of activation was, in their own words, " . . . an extensive confluent area along the midline that includes the lateral hypothalamic area, septal area, ventral striatum-substantia innominata, infralimbic cortex, prelimbic and orbitofrontal and the anterior cingulate cortex . . . Much of this is bilateral" (p. 198). The authors suggest that an important function of REM sleep is the integration of neocortical function with basal forebrain and hypothalamic motivational and reward mechanisms.

3.1.3. Selective deactivation of the dorsolateral prefrontal cortex in REM sleep. Relevant to the cognitive deficits in self-reflective awareness, orientation, and memory during dreaming was the $H_2{}^{15}O$ PET finding of significant deactivation, in REM, of a vast area of dorsolateral prefrontal cortex (Braun et al. 1997; Maquet et al. 1996). A similar decrease in cerebral blood flow to frontal areas during REM has been noted by Madsen et al. (1991a) using single photon emission computed tomography (SPECT) and by Lovblad et al. (1999) using fMRI. Dorsolateral prefrontal deactivation during REM, however, was not replicated by an FDG PET study (Nofzinger et al. 1997) and this discrepancy, therefore, remains to be clarified by other FDG as well as $H_2{}^{15}O$ studies. (A potential cause of this discrepancy arising from differences between FDG and $H_2{}^{15}O$ methods is discussed further in sect. 3.3.5.2.)

Nevertheless, it seems likely that considerable portions of executive and association cortex active in waking may be far less active in REM, leading Braun et al. (1997) to speculate that "REM sleep may constitute a state of generalized brain activity with the specific exclusion of executive systems which normally participate in the highest order analysis and integration of neural information" (p. 1190).

Taken together, these results strongly suggest that the forebrain activation and synthesis processes underlying dreaming are very different from those of waking. Not only is REM sleep chemically biased but the preferential cholinergic neuromodulation is associated with selective activation of the subcortical and cortical limbic structures (which mediate emotion) and with relative inactivation of the lateral prefrontal cortex (which mediates directed thought). These findings greatly enrich and inform the integrated picture of REM sleep dreaming as emotion-driven cognition with deficient memory, orientation, volition, and analytic thinking.

The Maquet et al. (Maquet et al. 1996; Maquet & Franck 1997), Nofzinger et al. (1997), and Braun et al. (1997) groups all stress that their findings suggest assigning REM sleep a role in the processing of emotion (along with its cognitive and autonomic correlates) in memory systems via a limbic-cortical interplay. Additionally, PET researchers suggest the possible origin of dream emotionality in REM-associated limbic activation (Braun et al. 1997; Maquet & Franck 1997) and dream-associated executive deficiencies in REM-associated frontal deactivation (Braun et al. 1997; Maquet & Franck 1997). Although tantalizing correlations such as: (1) limbic activation and dream emotionality, (2) dream emotionality and affect-congruent dream narratives, and (3) frontal deactivation and dream bizarreness, are now becoming apparent in the sleep and dream literature, the precise causal sequence among these phenomena remains to be established by future research.

Two additional findings support this proposed corticolimbic interaction. First, the anterior cingulate cortex has consistently shown increased activation in REM in other PET studies (e.g., Bootzin et al. 1998; Buchsbaum et al. 1989; Hong et al. 1995). Second, recent studies of human limbic structures with depth electrodes during REM sleep have shown distinctive rhythmic EEG patterns possibly related to the REM-associated hippocampal theta rhythms seen in animals (Mann et al. 1997; Staba et al. 1998). Human frontal midline theta has also been detected using scalp electrodes (Inanaga 1998).

3.1.4. Global and regional decreases in activation level in NREM sleep. Neuroimaging studies also strongly support a distinction between REM and NREM sleep as states whose differing neuroanatomical activation patterns predict their observed phenomenological differences (Table 2). PET studies of NREM sleep generally show a decrease in global cerebral energy metabolism (i.e., O_2 or glucose utilization) relative to waking and REM (Buchsbaum et al. 1989; Heiss et al. 1985; Madsen & Vorstup 1991; Madsen et al. 1991b; 1999b; Maquet 1995; Maquet et al. 1990; 1992; 1997). The magnitude of this decline relative to waking has varied from 11% glucose utilization in stage 2 (Maquet et al. 1992) to 40% glucose utilization in stages 3 and 4 (Maquet et al. 1990). A similar pattern has usually been reported for global cerebral blood flow as measured by $H_2{}^{15}O$ PET, SPECT, near infrared spectroscopy or a modification of the Kety-Schmidt O_2 uptake technique (Braun et al. 1997; Hoshi et al. 1994; Madsen et al. 1991a; 1991b; Maquet et al. 1997; Meyer et al. 1987; Sakai et al. 1980), although some studies have failed to show this global hemodynamic change (Andersson et al. 1995; 1998; Hofle et al. 1997). In addition, cerebral energy metabolism decreases with progressively greater depth of NREM sleep (Maquet 1995) a result recently replicated with fMRI (Sutton et al. 1997). By contrast, in REM, global cerebral energy metabolism tends to be equal to (Asenbaum et al. 1995; Braun et al. 1997; Madsen et al. 1991b; Maquet et al. 1990) or greater than (Buchsbaum et al. 1989; Heiss et al. 1985) that of waking. Cerebral blood flow velocity measured in the middle cerebral artery similarly shows a slowing during NREM followed by values similar to waking during REM (Droste et al. 1993; Haiak et al. 1994; Klingelhofer et al. 1995; Kuboyama et al. 1997).

More striking than global patterns are the now well-replicated regional variations in cerebral energy metabolism over the wake-NREM-REM sleep cycle (Table 2). Earlier studies showing specific declines in thalamic glucose utilization in NREM relative to waking (Buchsbaum et al. 1989; Maquet et al. 1990; 1992) have been confirmed by recent oxygen utilization studies (Andersson et al. 1998; Braun et al. 1997; Hofle et al. 1997; Maquet et al. 1997). In addition to prominent thalamic deactivation, all three recent studies have found regional deactivation during NREM in the pontine brain stem, orbitofrontal cortex, and anterior cingulate cortex (Braun et al. 1997; Hofle et al. 1997; Maquet et al. 1997). NREM deactivation of lateral prefrontal cortex was also observed in some studies (Andersson et al. 1998; Braun et al. 1997). Thalamic activation was found to decline significantly concomitant with increased delta EEG activity and there was an additional decline associated with increased spindle-frequency activity when the decrements associated with delta were subtracted (Hofle et al. 1997). (For a very recent review see Maquet 2000.)

Table 2. *Review of relative activation of cortical and subcortical areas in REM and SWS noted in four recent PET studies (from Hobson 1998a; 2000)*

SLEEP STAGE	REM	REM	REM	REM	NREM (3&4)	NREM (delta)	NREM (3&4)
STUDY	Maquet et al. 1996	Nofzinger et al. 1996	Braun et al. 1997	Braun et al. 1997	Maquet et al. 1997	Hofle et al. 1997	Braun et al. 1997
TECHNIQUE	$H_2{}^{15}O$	^{18}FDG	$H_2{}^{15}O$	$H_2{}^{15}O$	$H_2{}^{15}O$	$H_2{}^{15}O$	$H_2{}^{15}O$
RELATIVE TO	all other stages	waking	pre- (& post*)-sleep waking	NREM 3&4	all other stages	change with increased delta	pre- or post-sleep waking
SUBCORTICAL AREAS							
brainstem							
pontine tegmentum	increase		increase (R*)	increase	decrease	decrease:R	decrease
midbrain			increase*	increase			decrease
dorsal mesencephalon	increase				decrease		
diencephalon							
thalamus	increase: L			increase	decrease	decrease: M	decrease
hypothalamus		increase: R, Lat.	increase: A-POA	increase: A-POA	decrease		decrease: A-POA
basal forebrain					decrease		
limbic system							
left amygdala	increase	increase					
right amygdala	increase						
septal nuclei		increase					
hippocampus			increase*	increase			
basal ganglia/striatum							
caudate		increase: A, I, L	increase*	increase	decrease		decrease
putamen				increase			decrease: P
ventral striatum (n. accumbens, sub.innominata)		increase		increase			decrease
lenticular nuclei					decrease		
cerebellum			incr. (vermis)*	increase (vermis)		decrease	decrease: I

SLEEP STAGE	REM	REM	REM	REM	NREM (3&4)	NREM (delta)	NREM (3&4)
STUDY	Maquet et al. 1996 $H_2{}^{15}O$	Nofzinger et al. 1996 ^{18}FDG	Braun et al. 1997 $H_2{}^{15}O$	Braun et al. 1997 $H_2{}^{15}O$	Maquet et al. 1997 $H_2{}^{15}O$	Hofle et al. 1997 $H_2{}^{15}O$	Braun et al. 1997 $H_2{}^{15}O$
TECHNIQUE RELATIVE TO	all other stages	waking	pre or post-sleep waking	NREM 3&4	all other stages	change with increase delta	pre or post-sleep waking
CORTICAL AREAS							
FRONTAL		decrease: L, small areas increase: R					
dorsolateral prefrontal	decrease: L: 10,11,46,47 R: 8,9,10,11,46	increase	decrease: 46*				decrease: 46
opercular			decrease: 45*				decrease: 45
paraolfactory		increase					
lateral orbital		increase: 11,12	decrease: 11*		decrease: 11,25	decrease: R 11	decrease: 11
medial orbital							decrease: R
caudal orbital			increase	increase			decrease
gyrus rectus		increase					
PARIETAL							
Brodmann area 40 (supramarginal gyrus)	increase: R A 40 decrease: L 40		decrease: 40*			increase: L 40	decrease: 40
angular gyrus			decrease: 39*				decrease: 39
precuneus	decrease				decrease: 7		
cuneus					decrease: 19		
pericentral						increase: L 3/4	
TEMPORAL							
mesiotemporal					decrease: R 28		
middle		increase R				incr: A R,L 21	
posterior superior				increase: 22		increase: L 22	
inferior/fusiform			increase: 37,19 (post-sleep only)	increase 37,19			
OCCIPITAL		decrease: L, small areas					
medial						incr: R 17/18 incr: L 17	
post-rolandic sensory			increase				
LIMBIC ASSOCIATED							
medial (prelimbic) prefrontal		increase: R 32	increase: 10	increase: 10			decrease: 10
anterior cingulate	increase: 24	increase: 24	increase: 32*	increase: 32	decrease: 24,32	decrease: 24/32	decrease: 32
posterior cingulate	decrease: 31	dec.: R sm. areas	decrease*				
infralimbic		increase: 25					
insula		increase: L	decrease: P	increase: A I			decrease: A
parahippocampal		increase	increase: 37*	increase: 37			
entorhinal	increase	increase (in fusiform)					
temporal pole				increase: 38			decrease: 38

Abbr: L-left hemisphere; R-right hemisphere; A-anterior; P-posterior; C-caudal; M-medial; Lat.-lateral; I-inferior; S-superior; A-POA-anterior preoptic area; all numerals = Brodmann's area; sm.-small, dec.-decrease, inc.-increase.

Hofle et al. (1997) and Maquet et al. (1997) both interpret this pattern of decline as reflecting the progressive deactivation of the reticular activating system (RAS) that accompanies deepening NREM sleep. This deactivation leads to dysfacilitation of thalamocortical relay neurons, which allows the emergence of underlying thalamocortical oscillatory rhythms (Steriade & McCarley 1990a; Steriade et al. 1993a; 1993b; 1993c; 1993d; 1994; for recent reviews see Steriade 1997; 1999; 2000). GABAergic neurons of the thalamic reticular nucleus then further hyperpolarize and dysfacilitate thalamic relay neurons as NREM deepens (Steriade et al. 1994). In this hyperpolarized condition, thalamic neurons become constrained to burst firing patterns first in spindle (12–14 Hz) and later in delta (1–4 Hz) frequencies as NREM deepens from Stage 2 to delta sleep (Steriade et al. 1993a; 1993d). The cortex may further constrain these spindle and delta-wave-generating thalamocortical bursts within a newly described slow (<1 Hz) oscillation seen in cats (Steriade et al. 1993a; 1993b; 1993c; 1993d) and humans (Achermann & Borbely 1997). In conclusion, the metabolic decline seen during NREM is centered on the central core structures (brain stem, thalamus) which are known to play a role in generation of the slow oscillations of NREM sleep (Maquet 2000; Maquet et al. 1997).

The regional pattern of deactivation in NREM, therefore, sharply contrasts with the regional *activation* of these same regions (i.e., thalamus, pontine brain stem, anterior cingulate cortex) in REM (Braun et al. 1997; Maquet et al. 1996; Nofzinger et al. 1997). Details of these stage-related differences are shown in Table 2. Note that a recent cat study has shown a similar pattern of brain glucose metabolism in REM (Lydic et al. 1991a).

3.1.5. Interpreting the PET imaging results with respect to the psychophysiology of dreaming. According to PET researchers, regional activation during REM may reflect a specific activation of subcortical and cortical arousal and limbic structures for the adaptive processing of emotional and motivational learning (Maquet et al. 1996; Nofzinger et al. 1997). Such processing may, in turn, account for the emotionality and psychological salience of REM dreaming (Braun et al. 1997). Some support for this comes from a PET (glucose) study showing correlation between content-analyzed dream anxiety and medial frontal activation (Gottschalk et al. 1991a).

In summary, the markedly differing physiology of wake, NREM, and REM cerebral activation should be reflected in the respective phenomenology of mentation reported from these three conscious states. More particularly, the specific phenomenology of REM mentation may reflect the neurobiologically specific brain activation pattern. Nofzinger et al. (1997) conclude that "the current findings of increased limbic and paralimbic activation during REM sleep . . . as well as global, regionally nonselective cortical deactivation and decreased metabolism during NREM sleep, are generally supportive of the traditional notion that more story-like affect-laden dreams are more attributable to the REM sleep, than NREM sleep behavioral state" (p. 199).

3.1.6. Brain lesions resulting in loss or alteration of dreaming.

3.1.6.1. Solms's nosology for lesion-related disorders of dreaming. A set of findings and conclusions which have proved remarkably complementary to the neuroimaging results have been reached following a neuropsychological survey of 332 clinical cases of cerebral lesions as well as a review of 73 extant publications on the dreaming-related sequelae of cerebral injury (Solms 1997a). Using these welcome and long overdue neuropsychological data, Solms proposes a new nosology for the brain-lesion related disorders of dreaming.

In one syndrome, "global anoneria," total cessation of dreaming in patients (whose normal waking vision is preserved) results from either posterior cortical or deep bilateral frontal lesions. The posterior global anoneria syndrome results from lesions of the inferior parietal lobes in either hemisphere, with lesions to Brodmann's areas 39 and 40 being the most restricted damage sufficient to produce the syndrome. The anterior variant of global anoneria results from deep medial frontal damage resulting in the disconnection of the mediobasal frontal cortex from the brain stem and diencephalic limbic regions. In this syndrome, bilateral damage to white matter in the vicinity of the frontal horns of the lateral ventricles was the most restricted site causing the syndrome.

The nosological distinction of a second syndrome, non-visual dreaming, from syndromes of global cessation of dreaming, was first systematically formulated by Doricchi and Violani (1992). In this syndrome, termed "visual anoneria" by Solms (1997a), bilateral medial occipito-temporal lesions produce full or partial loss of dream visual imagery (again with normal waking vision). Among his own patients, a decrease in the "vivacity" of dreaming was reported by two patients with damage to the seat of normal vision in the medial-occipital-temporal cortex (especially areas V3, V3a, and V4 but not V1, V5, or V6). Notably, a correlate of visual anoneria was visual irreminiscence, the inability to produce mental imagery in waking. In addition, partial variants of visual anoneria exist which involve selective loss of particular visual elements (e.g., "kinematic anoneria" or "facial anoneria").

In addition to these two disorders of attenuated dreaming, Solms reported another interrelated pair of symptom complexes that combined increased frequency and intensity of dreaming. He suggested that increased vivacity and frequency of dreaming was associated with anterior limbic lesions while recurring nightmares are associated with temporal seizures.

3.1.6.2. Conclusions suggested by convergent PET and lesion findings. We believe that these findings map particularly well onto the neuroimaging findings on REM. For example, extrastriate visual cortex is activated during REM (Braun et al. 1997; 1998) and lesions to this region produce the distinctive dream deficits of full or partial visual anoneria (Solms 1997a). In contrast, the striate visual cortex is deactivated during REM (Braun et al. 1998) while lesions to this region do not affect dreaming (Solms 1997a). Similarly, the seat of spatial cognition in the inferior parietal cortex (BA 40) is activated in the right (but not the left) hemisphere during REM (Maquet et al. 1996) while damage to this region, especially on the right, is sufficient to produce global anoneria (Solms 1997a). Moreover, much of the lateral prefrontal area is deactivated during REM (Braun et al. 1997; Maquet et al. 1996), while lesions to this region do not affect dreaming (Doricchi & Violani 1992; Solms 1997a).

Two exceptions to this general correspondence involve lesions of the brainstem (for which Solms reports no attenuation of dreaming) and lesions of the rostral limbic system (for which Solms reports an accentuation of dreaming). In

the case of pontine lesions, we suggest that any lesion capable of destroying the pontine REM sleep generator mechanism would have to be so extensive as to eliminate consciousness altogether. We base this caveat upon the difficulty of suppressing REM by experimental lesions of the pons in animals. In the case of the rostral limbic system, we caution that lesions there could as well be irritative as destructive and that lesions in different areas of this functionally highly heterogeneous region (Devinsky et al. 1995) could produce dramatically different effects.

3.2. Reciprocal interaction: A neurobiological update

The discovery of the ubiquity of REM sleep in mammals provided the brain side of the brain-mind state question with an animal model (Dallaire et al. 1974; Dement 1958; Jouvet & Michel 1959; Jouvet 1962; 1999; Snyder 1966). While animal studies showed that potent and widespread activation of the brain did occur in REM sleep, it soon became clear that Moruzzi and Magoun's concept of a brain stem reticular activating system (Moruzzi & Magoun 1949) required extension and modification to account for the differences between the behavioral and subjective concomitants of waking and those of REM sleep (see Hobson & Brazier 1981).

3.2.1. Implications for dream theory. We take the theoretical position that it is the cellular and molecular level brain events to be discussed that bias the brain to produce the conscious state differences that contrast waking, NREM, and REM sleep. As we will point out in detail in section 4 when we develop the AIM model, the shift from aminergic dominance in waking to cholinergic dominance in REM lowers the probability that consciousness will be exteroreceptive, logical, and mnemonic while correspondingly raising the probability that consciousness will be interoceptive, illogical, and amnesic.

3.2.2. Behavioral state-dependent variations in neuromodulation. A conceptual breakthrough was made possible by the discovery of the chemically specific neuromodulatory subsystems of the brain stem (e.g., Dahlstrom & Fuxe 1964; for reviews see Foote et al. 1983; Gottesmann 1999; Hobson & Steriade 1986; Hobson et al. 1998; Jacobs & Azmita 1992; Lydic & Baghdoyan 1999; Mallick & Inoue 1999; Rye 1997; Steriade & McCarley 1990a) and of their differential activity in waking (noradrenergic and serotonergic systems on, cholinergic system damped) and REM sleep (noradrenergic and serotonergic systems off, cholinergic system undamped) (Aston-Jones & Bloom 1981; Cespuglio et al. 1981; Chu & Bloom 1973; 1974; Hobson et al. 1975; Jacobs 1986; Lydic et al. 1983; 1987; McCarley & Hobson 1975; McGinty & Harper 1976; Rasmussen et al. 1986; Reiner 1986; Steriade & McCarley 1990a; Trulson & Jacobs 1979).

3.2.2.1. The original reciprocal interaction model: an aminergic-cholinergic interplay. The model of reciprocal interaction (McCarley & Hobson 1975) provided a theoretical framework for experimental interventions at the cellular and molecular level that has vindicated the notion that waking and dreaming are at opposite ends of an aminergic-cholinergic neuromodulatory continuum, with NREM sleep holding an intermediate position (Fig. 2). The reciprocal interaction hypothesis (McCarley & Hobson 1975) provided a description of the aminergic-cholinergic interplay at the

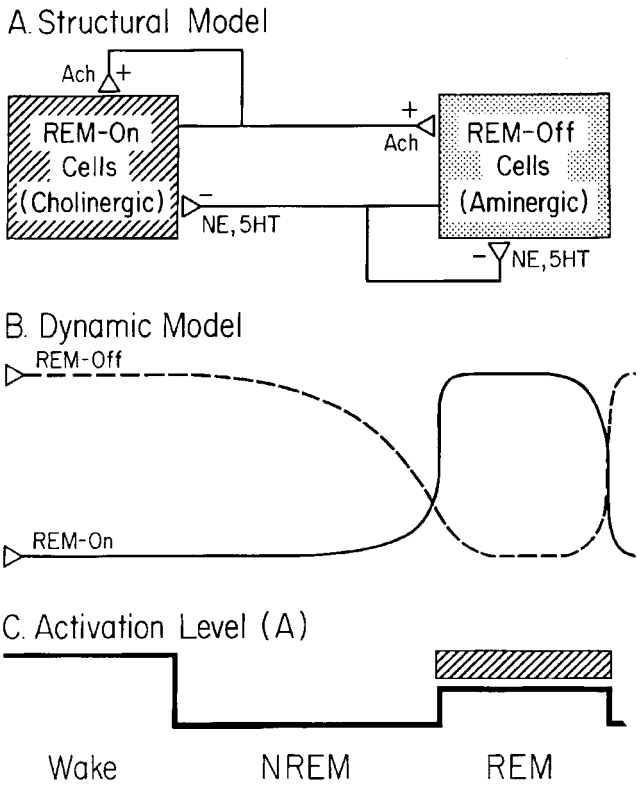


Figure 2. The original Reciprocal Interaction Model of physiological mechanisms determining alterations in activation level. A: Structural model of Reciprocal Interaction. REM-on cells of the pontine reticular formation are cholinoceptively excited and/or cholinergically excitatory (ACH+) at their synaptic endings. Pontine REM-off cells are noradrenergically (NE) or serotonergically (5HT) inhibitory (−) at their synapses. B: Dynamic Model. During waking, the pontine aminergic system is tonically activated and inhibits the pontine cholinergic system. During NREM sleep, aminergic inhibition gradually wanes and cholinergic excitation reciprocally waxes. At REM sleep onset, aminergic inhibition is shut off and cholinergic excitation reaches its high point. C: Activation level. As a consequence of the interplay of the neuronal systems shown in A and B, the net activation level of the brain (A) is at equally high levels in waking and REM sleep and at about half this peak level in NREM sleep. (Taken from Hobson 1992a.)

synaptic level and a mathematical analysis of the dynamics of the neurobiological control system (Figs. 2 and 3A). In this section we review subsequent work that has led to the alteration (Fig. 3B) and elaboration (Fig. 4) of the model.

Although there is abundant evidence for a pontine peribrachial cholinergic mechanism of REM generation centered in the pedunculopontine (PPT) and laterodorsal tegmental (LDT) nuclei (for recent reviews see Datta 1995; 1997b; 1999; Hobson 1992b; Hobson et al. 1993; Lydic & Baghdoyan 1999; Rye 1997), not all pontine PPT and LDT neurons are cholinergic (Kamodi et al. 1992; Kang & Kitai 1990; Leonard & Llinas 1990; 1994; Sakai & Koyama 1996; Steriade et al. 1988) and cortical acetylcholine release may be as high during wakefulness as during sleep (e.g., Jasper & Tessier 1971; Jimenez-Capdeville & Dykes 1996; Marrosu et al. 1995).

Recently, reciprocal interaction (McCarley & Hobson 1975) and reciprocal inhibition (Sakai 1988) models for control of the REM sleep cycle by brain stem cholinergic

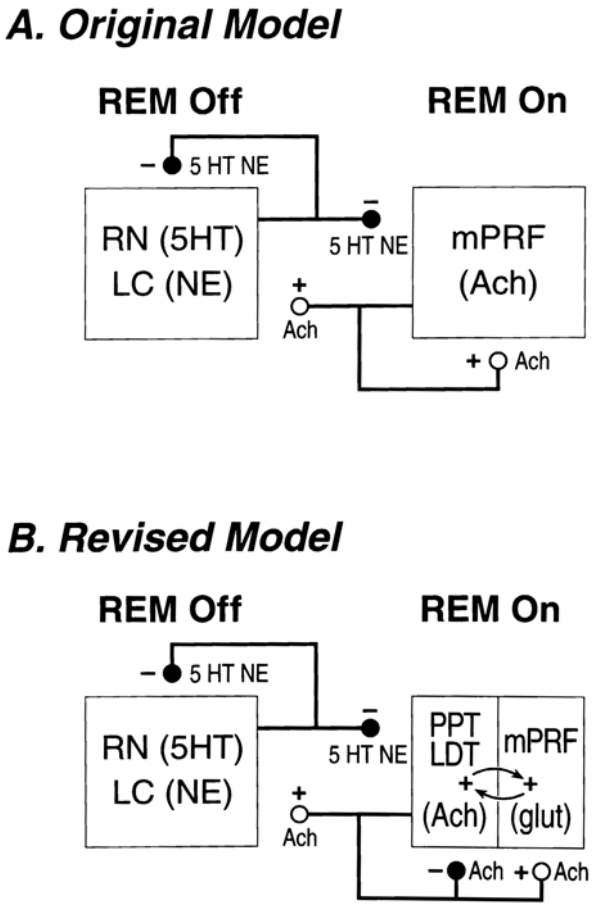


Figure 3. Synaptic modifications of the original reciprocal interaction model based upon recent findings. A: The original model proposed by McCarley and Hobson (1975) and detailed in Figure 2. B: Synaptic modifications of the original reciprocal interaction model based upon recent findings of self-inhibitory cholinergic autoreceptors in mesopontine cholinergic nuclei and excitatory interactions between mesopontine cholinergic and noncholinergic neurons (see Fig. 4 for more detail and references). Note that the exponential magnification of cholinergic output predicted by the original model (Fig. 2) can also occur in this model with mutually excitatory cholinergic-noncholinergic interactions taking the place of the previously postulated, mutually excitatory cholinergic-cholinergic interactions. In the revised model, inhibitory cholinergic autoreceptors would contribute to the inhibition of LDT and PPT cholinergic neurons, which is also caused by noradrenergic and serotonergic inputs to these nuclei. Therefore the basic shape of reciprocal interaction's dynamic model (illustrated in Fig. 2B) and its resultant alternation of behavioral state (illustrated in Fig. 2C) could also result from the revised model. *Abbreviations:* open circles, excitatory postsynaptic potentials; closed circles, inhibitory postsynaptic potentials; RN, dorsal raphe nucleus; LC, locus coeruleus; mPRF, medial pontine reticular formation; PPT, pedunculopontine tegmental nucleus; LDT, laterodorsal tegmental nucleus; 5HT, serotonin; NE, norepinephrine; Ach, acetylcholine; glut, glutamate.

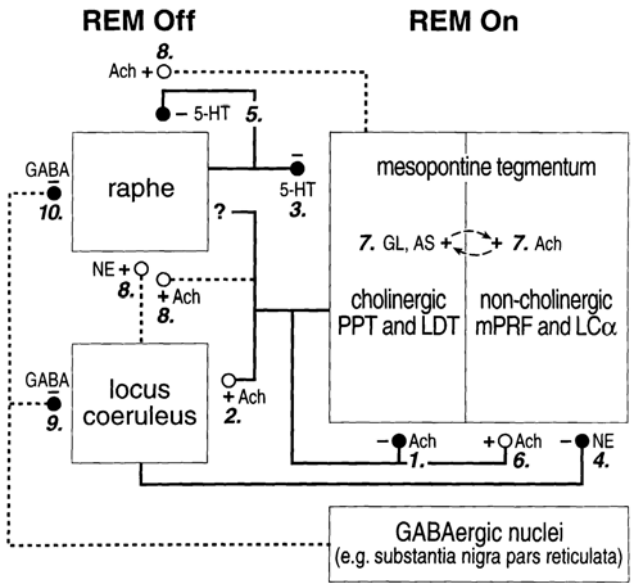


Figure 4. Additional synaptic details of the revised reciprocal interaction model shown in Figure 3B derived from data reported (solid lines) and hypothesized relationships suggested (dotted lines) in recent experimental studies (numbered on Figure and below). See text for discussion of these findings. Additional synaptic details can be superimposed on the revised reciprocal interaction model without altering the basic effects of aminergic and cholinergic influences on the REM sleep cycle. Excitatory cholinergic-non-cholinergic interactions utilizing Ach and the excitatory amino acid transmitters enhance firing of REM-on cells (6, 7) while inhibitory noradrenergic (4), serotonergic (3), and autoreceptor cholinergic (1) interactions suppress REM-on cells. Cholinergic effects upon aminergic neurons are both excitatory (2), as hypothesized in the original reciprocal interaction model and may also operate via presynaptic influences on noradrenergic-serotonergic as well as serotonergic-serotonergic circuits (8). GABAergic influences (9, 10) as well as other neurotransmitters such as adenosine and nitric oxide (see text) may contribute to the modulation of these interactions. *Abbreviations:* open circles, excitatory postsynaptic potentials; closed circles, inhibitory postsynaptic potentials; mPRF, medial pontine reticular formation; PPT, pedunculopontine tegmental nucleus; LDT, laterodorsal tegmental nucleus; LCα peri-locus coeruleus α; 5HT, serotonin; NE, norepinephrine; Ach, acetylcholine; GL, glutamate; AS, aspartate; GABA, gamma-aminobutyric acid. *References:* (1) Baghdoyan et al. 1997; El Manseri et al. 1990; Kodama & Honda 1996; Leonard & Llinas 1990; 1994; Luebke et al. 1993; Roth et al. 1996; Sakai & Koyama 1996; Sakai et al. 1990. (2) Egan & North 1985; 1986b. (3) Horner et al. 1997; Leonard & Llinas 1994; Luebke et al. 1992; Thakkar et al. 1997. (4) Sakai & Koyama 1996. (5) Portas et al. 1996. (6) Sakai & Koyama 1996; Sakai & Onoe 1997; Vanni-Mercier et al. 1989; Yamamoto et al. 1990a; 1990b. (7) Greene & McCarley 1990; Leonard & Llinas 1994; Sakai & Koyama 1996. (8) Li et al. 1997. (9) Nitz & Siegel 1997; Datta 1997b; Datta et al. 1991. (10) Porkka-Heiskanen et al. 1997a (from Hobson et al. 1998b).

and aminergic neurons have been questioned (Leonard & Llinas 1994). Specifically, the self-stimulatory role of acetylcholine on pontine PGO-bursting neurons has not been confirmed in *in vitro* slice preparations (Leonard & Llinas 1994). For example, ACh has been shown to hyperpolarize cell membranes in slice preparations of the rodent parabrachial nucleus (Egan & North 1986a), LDT (Leonard & Llinas 1994; Luebke et al. 1993), and PPT (Leonard & Llinas 1994). Similarly, LDT and PPT neurons with burst discharge properties most like those hypothesized to occur in PGO-burst neurons ("type I" neurons) may not be cholinergic (Leonard & Llinas 1990). Much evidence remains, however, that the reciprocal interaction model accurately describes essential elements of REM sleep cycle control even though some of its detailed synaptic assumptions need correction (Fig. 3B).