

# Sleep and Mental Illness

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Edited by  
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To our families  
who continue to support us selflessly and  
unreservedly in this and  
all our personal and professional endeavors.

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# Foreword

## Sleep as a model for mental illness

Sleep is a normal state that contains within it another normal state, dreaming. Dreaming shares with so-called “mental” illness the formal properties of psychosis (hallucinations and delusions) and is, by definition, a delirium (because it manifests visual hallucinations, disorientation, memory loss, and confabulation). So sleep is at the very least a model for mental illness. But sleep is certainly more than a model because it makes us think about what mental illness may really be. In so doing, it makes some of us realize that the term “mental illness” is really a misnomer. If we were more critical and more philosophical, we would substitute a definition like “diseases of the mind, the brain basis of which is not yet known.”

Practically all of the so-called mental illnesses discussed in this book fit this cumbersome definition. They are diseases of the mind, the brain basis of which is not yet known. But dreaming, that normal model of mental illness, has a brain basis that is becoming increasingly well known. And as its brain basis is better and better detailed, its distinctive mental manifestations are increasingly ascribable to an equally distinctive brain physiology. Thus we might suggest, not altogether facetiously, that dreaming is a brain–mind state whose psychological features are a direct expression of altered brain physiology. In other words, dreaming is a state of mind, the brain basis of which is now, in part, known.

If this is true (and I will publicly debate with anyone who says it is not true), then there is no such thing as mental illness without an underlying brain illness. That being the case, such a term as mental illness is a misnomer. We had better refer to diseases (or if you prefer, disorders) of the mind whose brain basis is not yet known and turn our attention to the scientific investigation of the brain in those conditions.

One way to begin such an enterprise is to study sleep and mental illness. This is just what is done in this book. Since we know a great deal about the brain

basis of sleep, we may be in a position to infer the brain basis of mental illness from observed changes in sleep. Let us look at several examples.

It is already clear that the aminergic neuromodulators mediate waking and, in order to go to sleep – and especially to dream – we need to be able to inhibit them powerfully. This is true of serotonin, norepinephrine, and histamine. The release of these neuromodulators throughout the brain decreases at sleep onset and is completely shut off in rapid eye movement (REM) sleep. That may be why dreaming, the psychological (or mental) concomitant of REM sleep, so faithfully simulates organic delirium. Organic delirium, after all, is commonly associated with toxic conditions that interfere with aminergic neuromodulation. I am referring to conditions such as delirium tremens, amphetamine psychosis, and other drug-induced states.

Major affective disorders similarly show aminergic abnormalities akin to REM sleep. In depression, we find reduced REM sleep latency and increased REM P1 intensity and duration. Most theories of depression postulate diminished aminergic synaptic efficacy and many drugs that are used to treat depression enhance aminergic synaptic efficacy. At the same time, and in keeping with the sleep as mental illness model, cholinergic mechanisms are enhanced, in both depressive and REM sleep. So why is the depressive affect seen so seldom in dreaming? Possibly because REM sleep only lasts minutes whereas depression lasts for weeks, months, and even years. The downstream effects of the similar neuromodulatory profiles may be quite different.

What about schizophrenia? It is phenomenologically even more different from dreaming than major affective disorder. The hallucinations are usually auditory and less commonly visual; the delusions are commonly paranoid, a feature that is very uncommon in dreaming. The flat affect that is so common in schizophrenia is never seen in dreaming. And the

pathophysiology has little in common with dreaming. Most theories of schizophrenia focus on dopamine, an aminergic modulator that changes little in sleep. So, by the time we get to schizophrenia (usually at the top of everyone's list), we seem far away from dreaming.

But, wait. There is still the fact that both conditions represent mental aberrations. So we should not close the door on our analogy too quickly and we certainly should not slam it shut. Two caveats come to mind: (1) the role of dopamine in sleep has been less well studied than the roles of serotonin, norepinephrine, and histamine; and (2) the mechanism of action of atypical antipsychotics (such as clozapine) may be related to enhancing effects on the aminergic neuro-modulators which are clearly sleep-wake efficacious.

The point of this foreword is to alert the reader to a strategic vantage point above the level of correlation appropriately taken by most of the chapters in this book. I am not saying that dreaming is a mental illness nor that mental illness does not exist. Instead, I am asserting that the proper scientific study of sleep considers it to be analogous to what we call mental illness, and those in sleep and dream science must strive to learn whatever we can about the brain's contribution to mental illness.

I am not arguing, either, for an eliminative materialism. That is to say, I recognize the contributions of problematical environmental surroundings to brain-mind health. And I certainly recognize the emotional salience of dreams, a salience that wise psychotherapists help their clients to appreciate. But I do seriously question what I consider to be the

exaggerated emphasis on the psychogenic causation of dreaming posited by psychoanalysis. This is not the place to take up my cudgel again against Freudian theory, but its fate at the hands of neurobiology may be a warning of what is to come as we further explore the brain basis of so-called mental illness.

A major problem confronting us in our scientific quest is the absence of good animal models for the functional psychoses. Because all mammals have REM, our task is made considerably easier when we study the brain basis of dreaming. But we have no good animal models for major mental illness. What are we to do? One answer is to use the modern techniques for the study of the human brain for all that they are worth, and then some. Quantitative electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) have already proven quite useful in discerning the brain underpinnings of such subtle mental states as lucid dreaming, which is distinctively different from both waking and dreaming (with both of which it shares features) so help may be on the way.

My introduction of the hybrid term brain-mind is meant to denote a step on the long road to a monism that never loses sight of the brain-mind nexus. In my crystal ball, brain is mind and mind is brain. They are two aspects of the same thing. Sleep, dreams, and what we now call mental illness are all functional states of the brain.

*J. Allan Hobson  
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## Preface

The idea for the first edition of this volume entitled *Sleep and Mental Illness* occurred to us when we published our earlier volume entitled *Sleep and Psychosomatic Medicine*. Mental disturbance is extremely common among those who suffer from sleep disorders. Despite the fact that a number of quality publications (including our own) exist on this increasingly popular research and clinical topic, each has certain gaps in coverage. We thus felt a need to address this deficiency by compiling one of the most comprehensive volumes ever published on sleep and mental illness. It has been an honor and privilege to edit this volume and to ensure that the necessary topics have been covered appropriately.

This volume is organized into three sections encompassing core topics in both sleep and mental illness as follows.

**Section 1** provides up-to-date background information on the basic science of this area of investigation. The topics included in this section are the neuropharmacology of mental illness, the effects of antidepressants on gene expression, and the neurochemistry of sleep. Other topics include the neuropharmacology of depression and animal models of sleep and stress. Also covered are chapters dealing with the relation between depression and insomnia and associated changes on levels of orexin in the brain.

**Section 2** covers the neuroendocrinological changes that are seen in pathophysiological states. These include the effects of disturbed sleep and depression on hormone secretion, sleep–endocrine relationships in depressed women across the reproductive cycle, and the relationship between melatonin and mental illness.

Finally, in **Section 3**, a series of clinical science topics relating to sleep and mental illness is presented. The range of clinical topics covered here represents the largest section of this volume. Starting with the International Classification of Sleep Disorders, this section addresses topics such as insomnia and the associated

risk for developing psychiatric illness in the future, antidepressant-induced alterations in sleep EEG, long-term effects of antidepressants on sleep, sleep during antipsychotic treatment, sleep and substance use and abuse, cognitive effects of psychoactive medications, and sleep-related memory consolidation in mental illness. Other topics include fatigue and sleepiness in affective illness, sleep in attention-deficit/hyperactivity disorders, sleep in seasonal affective disorder, and sleep in traumatic brain injury. This section also covers sleep and borderline personality disorders, sleep and eating disorders, sleep in late-life depression, and forensic issues of sleep in psychiatric patients.

This is an exciting time for specialists in both sleep and psychiatry. We have many reasons to be optimistic that significant progress is being made in the understanding, prevention, and management of sleep disorders. Our growing understanding of the pathogenesis and pathophysiology of mental illness, coupled with the rapidly expanding field of sleep medicine, has also seen the growth of an increasing number of successful management strategies. It is our hope that this volume will have a positive effect on the care of patients, especially those who present with comorbid conditions in current clinical practice.

The advent of sleep medicine has brought with it new perspectives on mental illness, and in particular a growing awareness that problems with sleep can both exacerbate and portend the development of mental disturbance in the future. Additionally, the impairment of the role of dreaming in affect regulation may be central to understanding the mood changes in depression. What this has meant is that psychiatrists are now discarding some long-cherished prescribing practices such as an increasing trend toward prescribing sleeping aids in addition to antidepressants.

Multidisciplinary care and a team approach are the best foundations for the effective practice of sleep medicine. It seems that the best approach to

Preface

comorbid sleep disorders is to involve a variety of experts in consultation as needed. This team approach should include consultations with psychiatrists, psychologists, behavioral sleep medicine professionals, and other sleep specialists. The management of comorbid insomnia symptoms in psychiatric patients can benefit greatly from the specialized knowledge of sleep professionals. It is the hope that advocacy of interdisciplinary care will promote excellence in the treatment of sleep disorders in mentally ill patients.

This volume is intended to be a resource for practitioners responsible for the care of sleep patients with mental illness and vice versa. That being said, this volume is appropriate for psychiatrists, psychologists, sleep specialists, and generalists alike. It can be useful for medical graduate students of biomedical and sleep medicine subspecialties. It will be also be of wide interest to others who want to get an overall grasp of sleep pharmacology and therapeutics and those physicians who evaluate and treat sleep disorders. In addition, the volume will be useful to clinicians of various disciplines who want to gain an overview of sleep psychiatry. This volume may serve as a reference work that will be of value to scientists and students alike. Since sleep disorders are almost

ubiquitous in clinical practice, we hope that you will find this material relevant and useful.

This volume includes contributions from a wide range of authors, many of whom are recognized internationally as authorities in their field. Overall, the reader may feel confident that the information presented is based on the old as well as most recent literature. Some of the information presented in this volume on older sedative hypnotics will be familiar to informed readers and will demonstrate to them how their previously acquired knowledge can be applied to the treatment of sleep disorders. Information about specific drugs may also be repeated in various chapters throughout this volume by very many authors. Inasmuch as repetition is the mother of learning, it is hoped that this redundancy will be construed as a benefit. The editors and authors would appreciate feedback on the contents of the volume with particular regard to any omissions or inaccuracies, which will be rectified in later editions. We also welcome your ideas, comments, and constructive criticisms, which are always appreciated.

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disciplines. To have found over 70 authors with a desire to contribute to the first edition could not have occurred without a tremendous concentration of effort and teamwork. Our publishing authors gracefully fulfilled our many requests, met our deadlines, and delivered their manuscripts accordingly, for which we are deeply grateful. We sincerely thank them for working with us through this long process. A number of individuals made outstanding contributions. A very special appreciation is also owed to several reviewers who made numerous helpful suggestions. Their candid comments and insights were invaluable.

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