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RESEARCH ON MENTAL ILLNESS AND ADDICTIVE DISORDERS:
Progress and Prospects

A Report by the
Board on Mental Health and Behavioral Medicine
Institute of Medicine

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NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the Councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the panel responsible for the report were chosen for their special competences and with regard for appropriate balance.

This report has been reviewed by a group other than the authors, in accordance to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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The Board wishes to thank those members of the Preparation Panel who prepared reviews of specific topics of interest and concern for internal use only (Appendix B).

Early in its deliberations, the Board also solicited comments from a wide range of experts throughout the biobehavioral sciences, especially researchers, clinicians, and educators in various disciplines who work in academic centers or research institutes throughout the United States. Each was asked to assess what research has achieved, what kinds of study are most promising or are needed most urgently, and what barriers seem to be hindering progress. The Board received 263 replies from a diverse sampling of biobehavioral scientists, providing a rich resource for its effort to synthesize a broad perspective of the field. The Board wishes to thank the many individuals who took time to provide such thoughtful and stimulating information.

The staff of the Division of Mental Health and Behavioral Medicine served the Panel and the Board in the development of this report. Peter Kramer, M.D., of the Department of Psychiatry, Brown University, was a consultant to the Division staff. The liaison function between the Board and the Alcohol, Drug Abuse, and Mental Health Administration was performed by Harold Pincus, M.D., the Special Assistant to the Director of the National Institute of Mental Health.

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Overview

This document is the response of the Board on Mental Health and Behavioral Medicine of the Institute of Medicine (IOM), National Academy of Sciences (NAS), to a request from the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). The Administrator asked the Board to: 1) review the current state of knowledge and opportunities for research within the ADAMHA mandate, 2) identify special needs for future research, and 3) assess benefits that already have accrued to public health in the United States from relevant clinical and basic research. In preparing its reply, the Board reviewed IOM and NAS documents on relevant areas (Appendix A) and solicited reviews of certain topics of special concern for its internal use only (Appendix B). In addition, the Board sought general appraisals of the field and received such assessments from several hundred scientists and clinicians throughout the country, representative of the full spectrum of fields relevant to ADAMHA.

With the reallocation several years ago of responsibility for clinical care delivery to states through block grants, the ADAMHA mission now centers on research and research training through its members: the National Institute of Mental Health (NIMH), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute on Drug Abuse (NIDA). As a logical aspect of its mission, ADAMHA also supports clinical training and disseminates research information to health professionals and the general public, to speed the transfer of new knowledge into practice.

This report briefly summarizes progress in understanding, preventing, and treating mental and addictive disorders and highlights some highly promising directions for further advances. Specific areas of focus are depression and mania, schizophrenia, anxiety and phobias, drug abuse, alcoholism, personality disorders, severe mental disorders of childhood and of old age, and the problems of chronic mental illness. The report also reviews ways in which a greater knowledge of behavior and brain function is increasingly relevant to major components of the current burden of physical illnesses, as investigators seek to identify health-damaging behaviors and to help people alter them.

The health consequences of the disorders and health-related behaviors in the ADAMHA domain are immense, as are related costs. Mental disorders and addictive states, especially when severe or chronic, cause personal, economic, and social upheaval both for afflicted individuals and for those close to them. In the United States alone, conservative estimates suggest that mental disorders and addictions directly afflict 30 to 45 million people and cost \$20 billion annually in direct health-care expenditures. They contribute especially to morbidity, using such measures as utilization of long-term care and Social Security Disability, and to indirect costs to society, including lost productivity, social services, and crime control. Overall, yearly direct and indirect expenses total an estimated \$185 billion. Costs are especially high for the severe mental problems of childhood, which can produce lifelong debilitation. These data suggest that economic consequences of the disorders under the ADAMHA purview are comparable to those for heart disease and cancer.

Interventions for many mental disorders and addictions have improved greatly over the past few decades, but they still typically only alleviate symptoms or induce remissions. The best way to lower total costs is to find ways to cure or, even better, to prevent these disorders; but much research is needed to attain this goal. Great progress is possible en route, as research yields better methods of early detection, clinical intervention, and rehabilitation for those suffering from mental illness, drug abuse, and alcoholism.

Each disorder entails a different mixture of psychological, social, and biological processes and of interactions among them. Therefore many different scientific disciplines are needed to contribute to advances on problems that ADAMHA addresses. Since the early 1950s, federal support has helped to create a cadre of skilled basic and clinical investigators in a wide range of these biobehavioral sciences who are eager to pursue many of the problems in the ADAMHA domain. However, the real buying power of research funding for mental and addictive disorders has dropped sharply during the past 15 years, even as available personnel and basic knowledge about behavior and about brain function have expanded dramatically. Steps now must be taken to reverse the adverse effects of reduced funding for research in these vital areas, which has greatly diminished career opportunities. Moreover, targeted training support still is needed to encourage talented scientists to enter some relatively understudied areas such as childhood disorders. In many ways, society can view support for this kind of work more as a capital investment than as an operating expense: the enormous personal and economic costs of these disorders are likely to decrease only as research yields more definitive treatment and preventive interventions.

Table I summarizes the main conclusions of this report, culminating in a call for a marked expansion of research support. The federal government has set a superb example in its research programs for several major physical disorders. Over the next 5 years, ADAMHA research allocations need to regain ground lost since the mid-1960s, to come more in line with the cost of mental and addictive disorders and with the readiness of the field for substantial progress. Research in many parts of the broad range of biobehavioral sciences is at an exciting and productive stage. Rapidly emerging information about brain function and about normal and abnormal behavior give hope that the invigorating effects of strong and sustained support soon will yield valuable dividends for the millions whose lives are touched by severe mental disorders, alcoholism, and drug addiction. Greater incentives for advancing this research not only are readily justified but imperative for the well-being of society.

TABLE I
MAJOR CONCLUSIONS

- o Mental disorders, alcoholism, and drug addictions profoundly disrupt the lives of 30 to 45 million people in the United States each year, with conservative estimates of annual expenditures for direct health care at \$20 billion and of total economic costs at \$185 billion.
- o Research already has improved drug and psychosocial therapies for some mental illnesses and addictions markedly; but much work remains to establish how to prevent, diagnose, and treat many of the most disabling problems. Some illnesses, including severe childhood mental disorders, alcoholism, and schizophrenia, typically have a costly, chronic course, so even relatively small advances can result in enormous direct and indirect savings for society.
- o Research on brain function and behavior is increasingly relevant to major physical disorders that contribute substantially to the burden of illness in the United States and other developed countries. Many of these diseases arise from specific unhealthy behaviors or require active, sustained cooperation for prevention or optimal treatment.
- o The amount of research on the disorders and health-related behaviors in the ADAMHA domain is much too low, given their enormous costs to society. Since 1966, the real level of federal support has dropped markedly, even as research opportunities and available scientific personnel have expanded.
- o Support for ADAMHA research and research training should undergo an orderly increase over the next five years. Several lines of reasoning converge to suggest that relatively conservative appropriate targets for levels of support would be, in constant 1983 dollars:

NIAAA, \$100 million; NIDA, \$100 million; NIMH, \$300 million.

The Magnitude of the Problem

The varied and overlapping disorders within the domain of the ADAMHA institutes are major contributors to the burden of illness in the United States. They attract less public attention than do some other disorders for a number of reasons, including their relatively low mortality rates and a stigma that many people attach to them. Still, both the chronicity of such disorders as schizophrenia, childhood psychoses, and some types of depression and the cascade of problems that can arise from others like alcoholism and drug abuse combine to produce enormous strains on affected individuals and on the health-care system. It is possible to assess the size of that effect in several ways.

The Number of People Affected

The people whose lives mental disorders and addictions touch offer one compelling measure of the impact these problems have on society. The following estimates are averages drawn from several reliable surveys of health problems in the United States.

The National Institute on Alcoholism and Alcohol Abuse (NIAAA) has as its immediate focus the 10 million adults and 3 million children and adolescents who abuse alcohol; another 30 to 40 million people are affected because of close family ties either with an alcoholic or with someone killed or injured by an individual who was under the influence of alcohol.

The National Institute on Drug Abuse (NIDA) initially studied illicit use and abuse of drugs; more recently, it has broadened its inquiries into mechanisms of addiction and habituation more generally, including those relating to cigarette smoking. Estimates of the number of drug abusers are imprecise, both because the activity is illegal and because of unresolved controversies over how to define drug abuse, as opposed to experimental or casual drug use. Still, the following estimates of drug abusers in the United States are illustrative: over 500,000 people are known heroin addicts; 5 million currently use cocaine; and at least 7 million regularly use prescription drugs, mostly addictive ones, without medical supervision. Recently, some groups have urged that the 44 million cigarette smokers in the United States who are unable to quit that habit also be included in such estimates of drug abuse; concerns about the appropriateness and value of this change are not yet settled.

The National Institute of Mental Health (NIMH), the oldest of the ADAMHA institutes, has the largest population of afflicted individuals. The overall prevalence of mental illness in the United States at any given time is about 15 percent, the most common severe disorders being schizophrenia and affective disorders. About 1 percent of the population will experience a schizophrenic episode sometime during their life, and about 300,000 episodes occur in the United States each year. Right now, affective disorders, including manic/depressive disease (bipolar affective disorder) and other types of depression, are disrupting the lives of 9 to 16 million people; less than a third of them will receive any form of treatment. About 15 percent of the population, or 30 million people, will experience at least one

serious bout of depression during their lifetime. Over 5 percent of the population now suffer from generalized anxiety, although most manage to continue to function and do not seek treatment. Obsessive compulsive disorder, affecting about 5 in 100,000 people, is relatively rare but is especially resistant to available treatments. Also of major concern to the mental health care system are the severe personality disorders; these typically chronic disorders hamper the lives of 5 to 10 percent of the general population and occur in about 20 percent of psychiatric inpatients.

The ADAMHA mandate covers a large range and number of people, though the total is not as large as the separate estimates might suggest. Some people are counted more than once because they have more than one problem, for example, depression and alcoholism or both alcoholism and multiple forms of drug abuse. Summarizing a variety of sources, the overall prevalence of mental and addictive disorders for all age groups in the United States is in the range of 15 to 22.5 percent. Thus, ADAMHA supports research of direct relevance to 30 to 45 million people. Included in this estimate are 2 million children with serious mental disorders in need of immediate care and another 8 to 10 million who have less severe but still distressing developmental difficulties. Also included are at least 10 percent of people over 65 years of age. These numbers can be compared with two other well-known major contributors to the burden of illness in the United States: 5 to 6 million Americans either know they now have cancer or have been treated for cancer at some time; 35 million have been told by a physician that they have a cardiovascular disease, and another 10 million have undiagnosed hypertension.

Costs to Society

Social costs offer a different but still distressing perspective of mental disorders and addictive states. None of the most common illnesses within this group have high direct rates of mortality, but many can lead to suicide, the tenth leading cause of death in the United States, with 30,000 reported deaths each year. Particularly disturbing is the trend in youth 15 to 24 years old: the suicide rate for this age group has increased from 5 in 100,000 in 1961 to 13 in 100,000 in 1983--a 150 percent increase. In addition to depression, other frequent precursors to suicide are alcoholism, drug abuse, and schizophrenia--all of which are within the ADAMHA mandate.

Disorders within the ADAMHA domain contribute indirectly to mortality in other ways. Thus, alcohol use leads to about 28,000 motor vehicle fatalities in the United States each year. Also, alcoholism is a risk factor for many physical disorders; on average, alcoholics live ten years less than nonalcoholics. Drug abuse can lead to violent death from suicide or homicide and puts users at risk of serious medical complications. The broader interface between behavior and health, which also lies partly within the ADAMHA purview, substantially increases these numbers; the United States Centers for Disease Control have estimated that long-term patterns of behavior, often called "lifestyle," contribute to 50 percent of the mortality from the 10 leading causes of death in this country.

Mental disorders and addictive states contribute substantially to morbidity in the United States. For example, they rank third for personal health care

expenditures, one major indicator of social cost (Table 2); this \$20 billion estimate does not include contributions these disorders make to costly physical disorders such as diseases of the digestive tract arising from alcoholism. Schizophrenia is an especially large source of health care costs. Even with available treatments, schizophrenics occupy over half the hospital beds for mentally ill or retarded patients and one quarter of all hospital beds in the United States. Schizophrenia accounts for 40 percent of all long-term care days, compared with 27 percent for cardiovascular disorders, and for 20 percent of Social Security Disability benefit days, exceeded only by cardiovascular diseases at 27 percent.

Because there are few effective treatments, severe childhood mental disorders often lead to lifelong and heavy use of many social resources. For example, residential treatment for one autistic child can cost more than \$30,000 a year, which means an outlay of well over \$1 million dollars during the expected normal lifespan.

TABLE 2
PERSONAL HEALTH CARE EXPENDITURES
FOR THE TEN MOST EXPENSIVE MEDICAL CONDITIONS
IN THE UNITED STATES IN 1980
(millions of dollars)

Medical Condition	All Ages	Under 65 years of age	65 years of age or over
Diseases of the circulatory system	\$33,184	\$13,078	\$20,015
Diseases of the digestive system	31,755	26,084	5,671
Mental disorders	20,301	14,612	5,689
Injury and poisoning	19,248	15,042	4,206
Diseases of the nervous system and sense organs	17,499	13,028	4,471
Diseases of the respiratory system	17,305	13,164	4,141
Diseases of the musculoskeletal system and connective tissue	13,645	9,821	3,824
Neoplasms	13,623	8,302	5,322
Diseases of the genitourinary system	13,162	10,721	2,441
Endocrine, nutritional, metabolic system and immunity disorders	7,656	4,689	2,968

Source: Division of Analysis, National Center for Health Statistics. National Center for Health Statistics: Health United States, 1983. Public Health Service. Washington, DC: US Government Printing Office, 1983. DHHS Publication No. (PHS) 84-1232.

There are 200,000 autistic children in the United States, and five times that many children have comparably severe forms of other pervasive developmental disorders.

Poor health of any kind produces costs to society that can far exceed those of direct health care and disability pay; examples of such indirect costs include lost productivity, restricted activity, and other types expenses that society incurs. Thus, estimated costs of opiate addiction, including losses from crimes, costs of law enforcement and private protection, prevention and treatment efforts, and welfare payments exceeded \$16 billion in 1977, the last year for which an estimate is available. A comparable analysis of the costs of alcoholism and alcohol abuse produced an estimate of \$43 billion for 1975. From this broader perspective of total economic costs to society, the overall impact of major mental disorders and addictive states on the United States economy is an estimated \$185 billion a year.

Many people object to efforts to calculate the indirect costs from an illness that arise from such effects as "lost productivity." They argue that this kind of estimate is inherently too imprecise to be useful, because of the number of assumptions that must be made, for example, how much someone would earn were he or she not afflicted with the disorder. Such exercises are of interest mainly because some illnesses, including chronic diseases and disorders of the young, contribute disproportionately to such measures, compared with such direct costs as personal health care expenditures. However, for mental disorders and addictive states, either the \$20 billion of personal health care expenditures or the \$185 billion of total economic cost amply document the point: these illnesses place an enormous drain on the United States economy.

Major Perspectives Within the Field

Many different scientific disciplines contribute to advances on problems that ADAMHA addresses. Each disorder entails a different mixture of psychological, social, and biological processes and of interactions among them. The term "biobehavioral sciences" is one rubric for the large and growing cluster of basic and clinical sciences that examine the intricacies of individual and group behavior and of brain function. Thus, the biobehavioral sciences include such basic disciplines as neuroscience, psychology, sociology, and anthropology; applied fields such as physiology and behavioral psychology; and the clinical specialties of psychiatry, psychology, psychoanalysis, social work, and psychiatric nursing. Also, developments within the field continue to spawn new subdisciplines such as behavioral genetics, sociophysiology, and psychoneuroimmunology. High-quality investigative efforts must remain aware of and open to multiple perspectives for studying brain function and behavior and for interpreting the results of such research.

Psychological Approaches

Psychology and psychiatry explore such topics as learning, motivation, and conscious and unconscious cognitive processes. Some basic and applied research in this area seeks to clarify how and why learning takes place, and how to facilitate it. Other work is directed toward delineating the nature and developmental course of the major building blocks from which individual personalities arise. Such information often is best couched in a developmental context, because the processes may change markedly over the life course. Ways in which they change with various physical and mental disorders constitute another fascinating and vital dimension. Quantitative techniques now permit precise and reproducible measures of a wide range of behaviors; assessments of character style and internal cognitive processes are more qualitative and less easily generalizable but also are beginning to yield to efforts to define them more precisely.

Psychological approaches are the basis of numerous treatments, among them psychoanalysis, brief psychotherapies, relapse prevention, crisis management, group therapy, cognitive therapy, hypnosis, and behavior therapy. Specific psychotherapies may be the treatment of choice, alone or together with an appropriate drug, for certain forms of depression, some phobias, and some addictions. Nondrug approaches may be especially advantageous at certain times in the life course, for example, early or late in life, when biological systems may be sensitive to drugs in unpredictable ways. In recent years, some psychotherapies have become more formalized, facilitating therapist training, making possible measures of minimum levels of mastery, and enabling researchers to examine how closely therapists adhere to theoretical standards in real treatment situations.

Substantial progress has been made toward increasing the scientific rigor of research on psychotherapy. In addition to the standardization of some psychotherapies, conceptual and technical advances have enhanced the description, measurement, and replication of critical aspects of the therapeutic process. For example, clinical researchers have improved diagnostic methods and created

objective scales to rate symptom severity and treatment outcome. Specific therapies now are being assessed not only on the basis of conceptual approach but also according to such parameters as speed and durability of response, patient acceptance, cost, and the scope of disorders to which they can be applied. Assessments of treatment outcome now can go beyond relief of the presenting complaint to broader evidence of internal and external changes, both positive and negative. Efforts also are being made to learn how to match specific types of problems or patients with particular therapeutic approaches. Furthermore, methodologists and statisticians are beginning to identify ways to examine the many existing psychotherapies from a broader perspective, seeking commonalities that eventually may lead to the formulation of general rules of how psychological interventions work, for whom, and with which disorders.

Research on how people acquire ideas and behaviors helps clarify the mechanisms by which individuals change behaviors and beliefs; the results are being applied to developing ways to help people abandon unhealthful habits and adopt more healthful ones. Social learning theories have been especially relevant to such efforts. One clear lesson from public health campaigns of the past several decades has been that simple transmission of knowledge is not enough. Rules for optimizing such efforts still are being defined empirically but already are yielding useful data both for designers of future programs and for theoreticians trying to understand how people adopt and alter specific habits. Various learning models also have been important in finding ways to optimize recovery from medical illnesses and in addressing the problems of chronic disability.

Social Science Approaches

Such basic social processes as forming relationships, establishing status hierarchies, behaving normatively, and conforming to social influences and expectations seem to be innate human characteristics that also occur in some nonhuman species. Many forms of mental and addictive disorders are associated with changes in such social processes, for which the social sciences have devised quantitative methods of study. Among the scholarly disciplines directly relevant to ADAMHA research and treatment interests are anthropology, ethology, economics, epidemiology, demography, social psychology, and sociology.

Social science analyses can be made at many levels, including small group, family, organization, community, larger society, and different cultures. Thus, organizations such as the workplace and schools can offer "natural experiments" for learning how systems shape and constrain what people do. Social sciences can provide both basic information and clinical applications. For example, they can define normal development and maintenance of basic social processes and how those processes change with a severe mental disorder. Thus, one cause of depression--bereavement--can be viewed as a social loss that markedly alters social roles and patterns. Social scientists have begun to struggle with the complex issues of how social loss is translated into depression and why social supports can buffer the effects of some illnesses.

Social structures that transmit normative values to new generations are of intense interest to social scientists. The impact of such widespread changes as working mothers, delayed families, and high divorce rates on family function can be assessed only if information is available about the family system. A body of clinical literature describes family dynamics and the key role that interrelationships within the family play in later functional and dysfunctional modes of relating among children and adults. Basic research can help to identify and classify possible kinds of relationships across the life cycle of the family; such work is the key to understanding the relative contributions such relationships make to the subsequent course of mental health or disorder. Both functional and dysfunctional family systems should be examined, to learn how they affect children in the areas of trust, self-acceptance, achievement, and responsibility. Information is needed especially of ways in which children can be helped to develop optimally even when they are exposed from an early age to the disrupting effects of mental illness or drug or alcohol abuse in the family. The children at most risk seem to be those directly involved in abnormal behavior in a family environment of discord and impaired communication. A family-system approach is intrinsically preventive: intervention in dysfunctional patterns of one generation can help prevent recurrent difficulties in future ones.

Basic knowledge of social processes also may help clarify a key behavioral change in schizophrenia, namely a decreased ability to function socially. Intriguing studies strongly indicate that schizophrenics are quite sensitive to certain aspects of their social environment. Their level of functioning and ability to stay out of the hospital without drugs improves markedly if they reside in a setting where they are not exposed to relatives who repeatedly express strong emotions. Recent work suggests that families can learn to identify and change unhelpful interactive patterns, with consequent improvement in the schizophrenic's course.

Social sciences also speak to the organization and distribution of care. Much remains to be learned about how community patterns help to determine who seeks care and at what stage of the illness. Numerous lines of research give reason to hope that a better understanding of such social forces could enhance the efficacy of the health care system and decrease its costs.

Biological Approaches

Many biological disciplines have important roles in research on mental illness and addictive states, including neurochemistry, neurophysiology, neuroanatomy, neuropharmacology, cell biology, analytical chemistry, and molecular genetics. These disciplines are linked together in the growing interdisciplinary field of neuroscience; new technologies emerging from them are applicable to many research problems within the ADAMHA mandate.

Neuroscientists now can isolate and identify a diverse range of substances that nerve cells use to maintain function and communicate with each other. In the past thirty years, details about how the brain works have become available far more rapidly than anyone could have guessed. Methods ranging from highly specific antibodies to physical probes of membrane fluidity give information on the

properties of specific types of brain cells. New analytic techniques such as high performance liquid chromatography, radioimmunoassay, and mass spectrometry have markedly improved detection, characterization, and measurement of substances in the nervous system. Nerve cell growth and maturation also can be studied. Simplified models of neural function exist, and some aspects of message generation and transmission are known with impressive detail. It now is clear that an unexpectedly rich variety of neurotransmitters and other types of neuroregulators play a role in communication systems within the brain; probably only a fraction of them are known, as yet.

Much current excitement comes from an increased ability to understand the biology of the cells of the brain and the molecular processes they use to communicate with and regulate each other. New methods for tracing circuits in the brain and determining the molecular mechanisms underlying the transfer of information among nerve cells have greatly enhanced knowledge about the ways in which the brain receives and processes information. Biochemical techniques for tracing specific neuroanatomy not only have helped clarify how neurons communicate but also have fostered the development of new methods of assessing and treating disorders of the brain and of behavior. Also exciting is evidence that it may be possible to make functional neuronal implants in certain parts of the brain, raising the possibility of replacing damaged tissues in some select cases.

Much useful information on the cellular properties of the nervous system is being gained through cell cultures and other in vitro preparations. Increasingly, genetic mutants are used to study the functional role of various neuroregulators and brain structures and as models of certain disease states; typically, such mutants are selected on the basis of an observable behavioral or neurological deficit and then studied for their underlying chemical or structural defects. Molecular biology, including recombinant DNA techniques, are useful for discovering new transmitters and hormones and obtaining the genes for receptors and enzymes that control them. These, in turn, hold great promise of facilitating the design of more specific drugs that have fewer and less unpleasant side effects. It also may lead to the development of specific probes for the diagnosis or even alleviation of disease.

Animal models have been and continue to be valuable aids in research on mental and addictive disorders. Learning models enable researchers to study learning acquisition and related processes; even simple life forms such as single-cell organisms and invertebrates have much to offer in this regard. Other animal models permit studies of emotional behaviors and of certain aspects of human disorders, including depression, psychosis, and drug addiction.

In recent years, the ability to monitor brain function in living animals and intact human beings has expanded greatly. The range extends from studying the activity of single nerve cells in animals to monitoring regional metabolic activity in human beings. Among the new research tools are the brain imaging techniques such as x-ray computed axial tomography (CAT), positron emission tomography (PET), and nuclear magnetic resonance (NMR); methods of recording brain electrical activity without having to insert electrodes into brain tissue, so-called "noninvasive recording"; and direct measures of brain function, including event-related electrical

potentials and quite recently in vivo metabolic NMR spectroscopy. Many of these recently conceptualized techniques have become feasible only now because of advances in mathematical and computer technologies, creating affordable and rapid methods to collect and process the typically large amounts of data involved. Together, these research tools are creating unparalleled opportunities to ask questions about specific changes in brain function that precede and arise from severe mental disorders and addictions.

Multidisciplinary Approaches

Few researchers find that their area of expertise is broad enough to answer many of the most fascinating questions about brain function, so the biobehavioral sciences are increasingly entwined in interdisciplinary research. Behavioral neurochemistry, which studies how behavior affects neurochemical events and how neurochemical events then alter subsequent behavior, is an example of an interdisciplinary pursuit. Such collaborations often foster substantial advances in the individual disciplines, as they are challenged to develop ways to assess specific aspects of brain activity or behavior without interfering with the techniques employed by the other specialties.

Certain disciplines span many approaches within the biobehavioral sciences. For example, epidemiology helps to mold intellectual concepts about disorders and also may shape the research agenda. ADAMHA's support of the catchment area studies is yielding irreplaceable data about mental disorders in the normal population. Determining the similarities and differences in the manifestations of schizophrenia across cultures also requires careful epidemiological studies, as do efforts to tease out relative contributions of its biological and psychosocial causes. Statistics is another field of universal importance to the biobehavioral sciences, as are population genetics and linguistics. For example, linguistics has facilitated studies of communication patterns in schizophrenics. Other scientific domains hold similar promise, even though, as yet, there have been few actual applications. Thus, mathematical modeling may greatly assist hypothesis formulation and testing.

Multidisciplinary approaches may be essential in answering some vital questions about individual susceptibility to mental illnesses and addictions. Powerful environmental and experiential factors appear to interact with poorly defined biological predispositions. Some of these abnormal expressions probably arise from maladaptive learning early in development. Clarification of the specific psychosocial and neurobiological bases of learning and memory should give valuable clues to their underlying behavioral and neural substrates. For example, investigators only recently became aware of the marked protection people gain from thinking that they can predict and control stressful events. This discovery already has shed light on the coping process and its connection to such mental illnesses as reactive depression and some forms of schizophrenia, but much remains to be learned about its neurobiological and neurophysiological concomitants. Similarly, some fascinating experiments contradict the longheld dogma that the brain has no regulatory control over the immune system. Researchers in the new field of psychoneuroimmunology examine the role of previously unsuspected links between the brain and the body's immune activities. These intriguing new per-

spectives of brain function highlight both the promise and the difficulties of interdisciplinary efforts. The needed research is complex and demands innovative approaches from experts in various fields, who often must work under conditions quite different from those to which they are accustomed. Yet, such studies, done with sufficient rigor and thoroughness to advance knowledge, are a challenge worthy of the best scientific minds.

Multidisciplinary approaches may be particularly fruitful in efforts to improve treatment interventions for mental disorders and addictive states. Psychosocial treatments may be synergistic with drug and other biological interventions. Thus, behavior therapy seems to enhance the effects of antidepressants in treating certain phobias, psychotherapy and attention to social milieu can improve the long-term outcome of medicated schizophrenic patients, and manic patients on lithium can benefit from adherence counseling. Clarification of potential positive and negative effects of interactions among various approaches is an important aspect of further multidisciplinary studies.

Perhaps even more than other types of large research efforts, multidisciplinary studies need an organizing focus. To succeed, collaborators must overcome major hurdles, as they seek to create a common bond among disparate disciplines. Over the years, ADAMHA has sponsored in major academic institutions some multidisciplinary clinical research centers that have proven remarkably effective at fostering such bonds. Unfortunately, only a few of these highly productive centers exist, but those are a national resource for research on mental disorders and addictive states.

Research Progress on the Major Disorders

The following disorders are illustrative of the research problems that ADAMHA addresses, of progress already made, and of some especially promising directions for further research. The disorders were chosen mainly because of the size of the populations that suffer from them and the contribution they make to the burden of illness in the United States; but, research on other mental disorders not discussed here also merit vigorous support. For example, the eating disorders anorexia nervosa and bulimia, which now afflict 1 to 2 percent of young women, can cause severe physical complications; information about their epidemiology, biobehavioral etiology, and treatment and prevention is needed urgently. Also, NIMH already supports useful studies of the psychological concomitants of the newly identified acquired immunity disorder syndrome (AIDS); among other potential benefits, such research may provide invaluable clues into the interconnections between the brain and the immune system.

Affective Disorders

The affective disorders, which include mania and the various forms of depression are probably the most destructive group of mental illnesses in the United States in terms of prevalence, mortality, economic cost, and impact on families. Appropriate use of antidepressant or antimanic drugs and psychotherapy can help about 80 percent of those afflicted; yet, less than one third ever receive treatment. Although the focus here is on manifestations of these disorders in young and middle-aged adults, affective disorders can strike people of all ages. There are pressing research questions about how affective disorders manifest themselves in childhood and adolescence and about the most useful early interventions in these young populations. Other clinical and research problems associated with depression in young and elderly age groups are discussed in later sections of this report.

Clinical Syndromes. "Depression" can refer either to a normal mood or to a serious disorder. The normal mood consists of the transitory feelings of sadness or discouragement that everyone has during difficult times in life. The depression syndrome presents with many symptoms, only one of which is sadness. Severely depressed people are profoundly pessimistic about the future and may feel unworthy of the good things in their lives. They may feel helpless and lose interest in work and social activities. Often, they feel excessive guilt about not meeting others' expectations. Some are anxious or fearful and may be physically active but accomplish little; others feel tired and weak, cannot concentrate, and move slowly. Among common physical symptoms in depression are headaches; backaches; stomach and intestinal distress; and, with severe depression, appetite and weight loss. Insomnia is another common problem, but suicidal thinking and attempts are the most dangerous symptom. In addition to its importance as a primary diagnosis, depression often can occur secondary to physical disorders. Conversely, a number of people who enter the health care system with complaints of a physical disorder actually are depressed.

Superficially, mania is the opposite of depression. Manic individuals may seem to be euphoric, overconfident, and carefree; often, they are optimistic and feel especially attractive, desirable, efficient, and alert. However, their mood typically is brittle and can deteriorate suddenly into irritability. Thought processes are disturbed, flitting from one idea to another. Delusions of special potency, knowledge, and abilities also can occur. Motor activity is accelerated; manics usually move restlessly from project to project, unable to complete any of them. Such symptoms can be devastatingly disruptive to personal relationships and careers.

The affective disorders generally have a waxing and waning course. Some people experience only a single bout of depression, but many have repeated episodes. Relatively few people have only manic episodes; more typical are the manic depressives, who cycle between mania and depression, with variable periods of normal mood in between. Several years ago, this syndrome was renamed "bipolar affective disorder," to emphasize its cyclic aspect. Other people have only unipolar depressions, never evincing any evidence of mania. Some never have full-blown episodes of either mania or depression but do have mood fluctuations that are independent of what is happening in their lives.

Treatment. Over the past 25 years, treatment of affective disorders has improved radically, with the discovery of effective antidepressant and antimanic drugs and development of improved psychosocial interventions. Proving the efficacy of such treatments was a challenge, because of the high rate of spontaneous remissions; the NIMH played an instrumental role by supporting that clinical research. Carefully controlled studies have shown that antidepressants and some forms of psychotherapy can relieve depression. As mentioned earlier, most acutely depressed patients respond to some combination of available pharmacological and psychotherapies. For many, treatments not only provide relief acutely but also can delay or prevent a return of symptoms.

Despite their success, antidepressant drugs are far from ideal. Their therapeutic effect begins only after two to six weeks, and they have numerous side effects that deter some patients from continuing to use them. An especially distressing feature of most available antidepressants is their toxicity. Their lethality at high doses makes the drugs especially dangerous for exactly those who need them most urgently--people with suicidal urges. Furthermore, antidepressants do not help everyone, and it is impossible to predict who will respond. Fortunately, those who fail to benefit from one type of antidepressant often respond well to another type. Electroconvulsive therapy (ECT) also is quite effective for some; but again there are unresolved concerns about potential side effects, particularly with repeated use. Similarly, the psychotherapies work for some but not all, take time to become effective, and may be least useful for precisely those patients most urgently in need. Distressingly, during the two to four months sometimes needed to find the right treatment, patients still suffer from their illness and are at risk of suicide.

The discovery that lithium salts have potent antimanic effects has been of great value to both clinical practice and basic science. Again, the NIMH had a key role in supporting clinical research that documented lithium's efficacy for treating mania

and bipolar affective disorder. Like the antidepressants, lithium can produce serious side effects and can be fatal in large doses.

Basic and Clinical Research. The advantages of a strong, diverse research base are manifest in several recent improvements in treatments of affective disorders. Thus, efforts to devise specific diagnostic categories have helped to identify more homogeneous subtypes of depression, thereby enhancing treatment efficacy. One subtype--bipolar affective disorder--has been found to have a strong genetic component and is especially responsive to lithium.

Most of the drugs that now are used to treat affective disorders were discovered serendipitously, often as a direct result of astute clinical observations. The drive to learn how these drugs work has led to major advances in understanding brain biochemical processes. Much remains to be learned, but research already done on the effects of antidepressants, lithium, and other psychoactive drugs has been instrumental in clarifying aspects of brain function.

Initially, attention focused mainly on substances called neurotransmitters, which transmit information from one nerve cell to another. More recently, scientists have learned that other substances, neuromodulators, can influence nerve cells more indirectly, for example by altering the release or actions of neurotransmitters. No consensus yet exists on a comprehensive nomenclature for the growing, increasingly varied group of compounds involved in brain function. The term chosen for this report, neuroregulators, denotes their common underlying purpose.

Basic research on neuroregulators includes identification and anatomical localization; studies of formation, utilization, and deactivation; and characterization of the sites of action such as receptors, the specific protein structure in cell membranes on which neurotransmitters act. Information about each of these aspects of neuroregulator function may be relevant to the problems of depression and mania, because antidepressant and antimanic drugs ultimately must act through a neuroregulator system. Studying neurochemical, physiological, pharmacological, and biobehavioral effects of such drugs may enable scientists to uncover the etiologies of the disorders and devise drugs for treating them more effectively and with fewer adverse side effects. In turn, identification of the involved neuroregulator systems should suggest new and more precise tools for prevention, diagnosis, and therapy.

Heuristic hypotheses about the role of neurotransmitters and other neuroregulators in mental disorders already exist for such well-known substances as dopamine, norepinephrine, serotonin, and acetylcholine. Most such hypotheses postulate that relatively excessive or deficient activity in a neuroregulator system produces the symptoms of a specific mental disorder. For example, in the mid-1960s, several groups proposed that norepinephrine was the key neurotransmitter in affective disorders, with low norepinephrine activity leading to depression and high activity producing mania. This hypothesis stimulated many innovative studies to elucidate the regulatory mechanisms that control norepinephrine activity; in turn, results of such work have led to refinements of the original hypothesis, for example, suggestions of a defect in the receptor. Analogous hypotheses exist for other neuroregulators, including serotonin and the

naturally occurring morphine-like substances called endorphins. Also of interest are suggestions that some forms of depression result from an imbalance among neuroregulators that usually work in balanced opposition to each other, rather than from an absolute abnormality in any one system. Tests and refinements of such hypotheses require more knowledge about regulatory mechanisms of brain neuroregulators of all types, ranging from well-known norepinephrine and serotonin to more recently discovered ones like histamine, epinephrine, and the endorphins and other neuropeptides. Important thrusts of current work include studies of neuroregulator synthesis, storage, release, inactivation, and receptors.

Studies of hormonal processes also are directly relevant to depression and mania. Many depressed individuals have changes in the function of the adrenal stress system and of the thyroid system. Such changes may prove to be disease markers that can be used to select the most effective type and length of treatment. Studies also suggest the importance in some types of affective disorders of physiological mechanisms for handling ions such as sodium and lithium.

Emerging techniques in molecular genetics and gene cloning also are likely to have applications to certain types of severe mental disorders within a few years. For example, such techniques recently were applied successfully to identify the chromosomal area involved in Huntington's chorea, a severe genetic disorder characterized by the development of dementia and uncontrollable writhing movements, usually in mid- or late life. This discovery opens a whole new range of approaches to uncovering the etiology of this devastating, poorly understood disorder, as scientists seek to isolate the genes involved and to determine how they are expressed biochemically. Analogous studies probably will be feasible in the near future for some disorders in the ADAMHA domain such as bipolar affective disorder, which also has a strong genetic component.

Some depressed patients have changes in their brain electrical patterns, including evoked responses and relative left/right hemispheric activity. Many experience marked alterations in sleep and biorhythms. For example, the first period of rapid eye movement sleep (REM or dream sleep) occurs earlier in the night in many depressed patients than for nondepressed controls. Some abnormalities resolve when the depression clears, potentially offering a sensitive and objective measure of the severity of the depression and the course of recovery. In an intriguing clinical observation about biorhythms, investigators recently identified a subgroup of patients who have seasonal depressions, seemingly as a response to a decrease in total sunlight; the depression lifts if these people either travel to a place with longer days or use appropriate lights to lengthen their days artificially.

Depression also has been the subject of extensive efficacy research for psychotherapies. Over the past ten years investigators have struggled with the difficult issues of designing adequate controls for psychotherapy research. A number of studies now have shown unequivocally that several psychotherapies are effective for depression. Although much more work is needed, research also indicates that certain types of psychotherapy are at least as effective as antidepressant drugs for some patients. Studies also suggest that a combination of psychotherapy and drug treatment can be superior to either form of treatment alone. There are intriguing indications that the two treatments augment each other because they work on

different target symptoms; extension of this work may provide useful clues about major components of the depressive syndrome.

Some types of depression are associated with stress, especially with losses. Studies of coping mechanisms, developmental processes, social behavior, and basic social processes can help to define the role of loss, other stresses, and social interactions in producing depression and influencing its course. Analyses of changes in social networks that accompany depression are essential. Such research can be done best in the context of fundamental exploration of the factors that mold coping patterns and patterns of social interaction, using both animal and human models of coping and learning. Available evidence suggests that the need to adapt to change, especially when the consequences are unpredictable and uncertain, may be relevant particularly to development of depression. Studies are under way to determine ways in which behavioral events can alter biochemical events and how those changed biochemical processes affect subsequent behavior.

Research is needed to identify which patients will be helped by what treatments or combination of treatments. As the number and diversity of effective drug and psychosocial interventions expand, clinicians will increasingly want objective, reliable criteria with which to match the patient to the optimal treatment modality and to monitor the response.

Schizophrenia

Traditionally, schizophrenia has been viewed as a profound deterioration in basic mental processes that carries a bleak prognosis. The situation has improved greatly over the past 30 years; many people with schizophrenia and other psychoses respond rapidly to a combination of existing drug and psychosocial interventions. Still, about 20 percent show no substantial improvement or experience side effects that make it impossible for them to continue on the drugs. Moreover, even among the many who do respond favorably to available interventions, improvement is often slow and incomplete; and those who do not respond typically face the prospect of a slow, downward course with repeated hospitalizations.

Clinical Syndrome. The confused, inappropriate, hallucinatory, and regressed behaviors seen in persons with schizophrenia have been recognized since the earliest times. The disorder usually begins with gradually increasing inner turmoil and a sense of ill-being, sometimes after a triggering situation or stress. As an episode evolves, more specific symptoms appear. Patients may be flooded with thoughts and fear they are losing control. Many begin to perform compulsive, painstakingly repetitious, often meaningless tasks. Further deterioration occurs in the form of increasingly severe distortions in perception, bizarre speech, and illogical thinking. Often, schizophrenics develop paranoid delusions that range from pervasive suspiciousness to unshakeable beliefs in complex, improbable plots against themselves or others. Emotional expression may be totally absent or markedly blunted. Many schizophrenics have hallucinations, but this is not an essential feature; if present, they usually are auditory, consisting of one or more voices that berate or threaten.

Treatment. Acute schizophrenic episodes typically respond to antipsychotic drugs and supportive psychosocial therapies. Taken together, data from many studies overwhelmingly confirm the ability of antipsychotic drugs to relieve some aspects of the schizophrenic syndrome, including the disturbed thought processes, hallucinations, and acute delusions; the drugs are much less useful for such "negative" symptoms as the emotional blunting and social isolation or for chronic delusions. These latter symptoms are more amenable to psychosocial interventions, arguing for a combined approach.

Antipsychotic drugs can produce many of the same minor side effects as the antidepressant drugs, although they typically are somewhat less toxic at high doses; however, they also can have additional, severe side effects, especially with long-term usage. An important group of side effects are the movement disorders, which can range from tremors to muscle rigidity or major involuntary muscle movements. Many of these effects resolve spontaneously or can be alleviated with other drugs; others are more troublesome and cause prolonged disability in some patients. An especially worrisome movement disorder is tardive dyskinesia, characterized by repetitive, involuntary writhing movements of the tongue, mouth, lips, body, arms, and legs. This sometimes irreversible disorder most often occurs after chronic treatment with antipsychotic drugs; however, little else is known about why it occurs or how to prevent it. There is intense basic and clinical interest in finding ways to separate the antipsychotic actions from those that produce the movement disorders.

The value of antipsychotic drugs for maintenance treatment is unresolved. These drugs can delay symptom recurrence in some patients, yet they have no benefit for others. At present, it is impossible to predict the needs of a given individual; yet the decision is an important one, particularly because of concerns about tardive dyskinesia with chronic administration. Objective methods of selecting who should stay on the drugs would greatly aid clinicians and their patients.

Psychosocial research is having a noticeable influence on the treatment of schizophrenia, with an increasing recognition of the substantial impact the hospital and community milieu can have on individual responses to drug therapy. If placed in supportive and emotionally undemanding settings, schizophrenics recover from an episode more quickly and remain in remission longer and with fewer drugs. Other psychosocial interventions include rehabilitation directed toward imparting work skills and promoting social adjustment. Many therapists now examine the patient's total social environment, helping both patient and family to recognize key psychological and social aspects of the disease and teaching them how to maximize supportive elements in the environment.

Basic and Clinical Research. As with the antidepressants, the clinical actions of antipsychotic drugs have generated a strong interest in how they work. Using available information about brain function, researchers have made several hypotheses about schizophrenia that have helped guide research in the area. The dopamine hypothesis postulates a relatively excessive activity in specific brain dopamine neuronal systems. Other hypotheses invoke abnormalities in neuropeptides or suggest an imbalance between neuroregulators that work in tandem. Tests of

these hypotheses require studies both of the neurochemical and neurophysiological events in key neural systems and of fundamental properties of neural networks. Mathematical modeling of neural networks may provide new perspectives on their functioning. Such work requires continued basic research support in neurobiology and psychopharmacology, on genetic aspects of neuroregulator function, on behavioral and biochemical interactions, and on neurophysiological and neuropsychological features of schizophrenia. Studies of the actions of drugs that mimic psychotic states and of agents used to treat them also provide research leads about the etiology of this disorder.

Studies now are being made of brain structure and function in living human beings. For example, x-ray computed axial tomography (CAT) enable researchers to examine some brain structures in detail. Although the work is at an early stage, some schizophrenics may have a decrease in brain volume. Similarly, early results with positron emission tomography (PET), which can monitor basic brain metabolic processes, suggest changes in specific brain regions of some patients with schizophrenia, compared with normal controls. Nuclear magnetic resonance (NMR), an emerging technique with the major advantage of not exposing subjects to possibly harmful ionizing radiation, eventually should permit both imaging and metabolic measures of the intact human brain. Electrophysiological studies of psychotic states have shown changes in REM sleep and in evoked responses to external stimuli. Computer analyses of the electroencephalogram (EEG) lend further support to the belief that some schizophrenics have a physiological deficiency in brain function. The emergence of such noninvasive methods promises a new era for studies of mental and addictive disorders of all types.

Schizophrenia is a heterogeneous collection of disorders, probably with multiple etiologies. Quite different disorders may produce similar symptoms, just as a fever and cough can arise from many causes. Clinical research is needed to establish more precise, homogeneous diagnostic categories. Ongoing studies involving every aspect of schizophrenia, ranging from genetic and biochemical to behavioral, should markedly enrich the information base needed to identify diagnostic categories with improved therapeutic and prognostic utility. Also needed is more research on the natural history of the disorder and on changes that occur with age. For example, many schizophrenics become less symptomatic as they become older. Among other uses, such studies would permit more realistic assessments of the long term efficacy of treatments.

Psychosocial research has provided vital information about epidemiological patterns of schizophrenia and its consequences; more work is needed, ranging from studies of how diagnostic labels affect patients and their families to the ways in which schizophrenia alters social processes. Much more must be learned in each psychosocial area, including how and why schizophrenia impairs language use and how it manifests itself in various cultures. Too little is known as yet about what people who later become schizophrenics are like during childhood and adolescence. Again, it would be invaluable to know whether early interventions can ameliorate or even prevent subsequent deterioration. Psychosocial techniques also could help to identify optimal environments for treating severely ill patients.

Anxiety Disorders

Anxiety may be defined as a painful uneasiness or a state of heightened tension accompanied by inexpressible dread, a feeling of unpleasant and apprehensive expectation, and a characteristic set of bodily symptoms. It often is accompanied by such physical symptoms as shortness of breath, nonproductive overactivity, hyperventilation, palpitations, chest pain, a sensation of choking or suffocating, nausea, abdominal pains, diarrhea, faintness, dizziness, blurry vision, headache, tremulousness, excessive sweating, and cold extremities. In contrast to fear, which usually occurs because of a perceived external danger, anxiety typically arises without an identifiable external threat that can account for the extent of the response. Recurrent episodes of anxiety are a chronic problem that constitute a disorder.

Anxiety can occur as part of many psychiatric disorders, including depression, schizophrenia, organic brain syndromes, senile dementia, and alcoholism and other substance abuse. Also, anxiety may accompany some physical disorders; and growing evidence suggests that it can worsen such dangerous illnesses as hypertension, heart disease and peptic ulcer. In addition, symptoms from some physical disorders, including hyperthyroidism and pheochromocytoma, may mimic or exacerbate anxiety.

Clinical Syndrome. Formally, anxiety disorders can be divided into five types; however, in reality, many people suffer from several clusters of these symptoms either sequentially or simultaneously.

Generalized anxiety disorder refers to a nonspecific anxiety state that persists for more than a month; often, but not always, the anxiety is associated with phobias or panic attacks.

Panic disorder refers to the occurrence of sudden, intense attacks of anxiety with both mental terror and severe physical symptoms; attacks last from minutes to, rarely, hours.

Phobic disorder is a persistent yet irrational fear of a specific object, activity, or situation, leading to an overwhelming desire to avoid the source of fear; real or anticipated exposure to the source of fear may produce panic attacks. Phobic disorders take many forms: agoraphobia is a marked fear of being alone or being in public places from which escape might be difficult; social phobia, a fear of humiliation and embarrassment in social situations; claustrophobia, a fear of closed places; acrophobia, a fear of heights. Simple phobias are fears of specific objects, often such animals as dogs, insects, snakes, or mice. Whatever the phobia, it can severely constrict an afflicted person's actions and come to dominate his or her life.

People who have obsessive-compulsive disorder are thought to master anxiety by associating it with repetitive unwanted thoughts or ritualistic acts, which then themselves become impossible to control. The syndrome has three common clinical presentations: 1) a persistent recurrence of distressing, uncontrollable, and unwelcomed thoughts; 2) an irresistible urge to perform certain repetitive acts; and 3) recurrent thoughts accompanied by a compulsion to perform a repetitive act.

Treatment of Anxiety Disorders. Over the past 25 years, there have been gratifying advances in treating anxiety disorders. Certain behavioral therapies are quite effective for many patients with anxiety disorders, especially some simple phobias. An early emphasis on systematic desensitization has been supplanted more recently by a variety of methods that have in common exposing the subject to the feared object or situation in a controlled setting.

The benzodiazepines, for example, diazepam (Valium) and chlordiazepoxide (Librium), can markedly diminish the acute manifestations of panic attacks for many people; they are much less effective in preventing a recurrence. In the past few years, a number of studies have shown that antidepressants also are effective for treating panic disorders and some phobias, even with patients lacking any evidence of depression. This finding raises provocative, unanswered questions not only about optimal treatment strategies for these disorders but also about possible links between affective and anxiety disorders.

Many patients do best on a combination of drug and psychotherapy, especially those with a longstanding generalized anxiety disorder. Yet, even combined approaches provide inadequate relief for some people with a severe anxiety disorder, particularly obsessive compulsive disorder. Their continued suffering speaks eloquently of the need for more research on both biological and psychosocial underpinnings of these difficult, debilitating disorders.

Basic and Clinical Research. Basic science advances in understanding anxiety have been striking. Within the past few years, investigators have learned that the brain contains specific receptors for benzodiazepines; these receptors probably help to regulate anxiety. The discovery of benzodiazepine receptors has prompted a search for naturally occurring brain substances that bind to them. That search, which is continuing, already has led to the discovery of several drugs that can produce anxiety through mechanisms which benzodiazepines can block. The inhibitory neuroregulator gamma-aminobutyric acid (GABA) also may play a major role in biological mechanisms relating to anxiety, as may the endorphins. Although the evidence is controversial, some investigators believe that an area deep in the brain called the locus ceruleus, which is known to be important in a number of behaviors, may have a key role in certain forms of anxiety. Careful studies of drugs that relieve and produce anxiety should help unravel this fascinating puzzle and suggest better ways to alleviate this major source of human suffering and debility.

Many questions about psychosocial aspects of the anxiety disorders need to be addressed. Given the impressive success of behavior therapies for some forms of anxiety, studies of underlying psychological mechanisms may yield valuable clues to the etiology of these disorders. For example, hypnosis is known to be an effective facilitator in such treatments, and good measures now exist to assess hypnotic susceptibility. Studies are beginning of factors that determine individual responsiveness and influence the utility of hypnotic suggestions for such pervasive problems as chronic pain, anxiety, conversion symptoms, phobias, and habit problems. Further research on hypnosis should clarify its utility in treatment and diagnosis. Careful examination also is needed of the familial and social contexts in which anxiety disorders develop. Social stress frequently is a precipitant of anxiety,

and many anxiety disorders such as agoraphobia and social phobias can be understood fully only with a thorough elucidation of the social processes that almost certainly help both to initiate and to maintain them.

Drug Abuse

Drug abuse is a major problem in the United States. At one level, it seems easier to understand than are many other public health problems: it entails voluntary self-administration of psychoactive substances, so the obvious "cure" is abstinence. Yet, this appealing view ignores the tenacity of drug use and abuse throughout human history and neglects the role of the drug user, who actively seeks to continue using drugs. Until recently, most attempts to control drug abuse have been legal efforts to block drug production or to punish users or dealers; research advances offer the promise of other, hopefully more effective, approaches to the problem. Successful attacks on drug abuse most likely will come from knowledge of the complex biological, psychological, and social factors that reinforce drug-seeking and drug-using behavior despite its dangerousness and destructiveness to users, their family members, and society.

The diverse variety of psychoactive drugs can be divided into five major classes: opiates, hallucinogens, marijuana, psychostimulants, and sedative hypnotics. Alcohol, which is a sedative hypnotic, is discussed separately, because of its unique standing in society. Opiate addiction serves as a good example of drug abuse, for purposes of this report.

Clinical Syndrome. Opiate addiction comes in many forms and occurs in all socioeconomic groups, though most addicts in the United States are young males. Because they experience especially intense effects that way, addicts graduate quickly to intravenous injections, usually of heroin. This highly addictive drug produces a euphoric state that temporarily frees the user from the problems of everyday life, and thus is a powerful reinforcer of its own use. For regular users, response to a given amount of opiate declines rapidly, so addicts must increase their dosage to gain the desired effects. This phenomenon, called tolerance, and the withdrawal symptoms that accompany acute cessation of the drug in someone who has developed tolerance, constitute a reasonable definition of addiction.

The concomitants of addiction depend greatly on the social circumstances of the addict. Many abusers lack sufficient legal income to support their habit and resort to crime to get money. In the United States, all available heroin is synthesized illegally, with no quality controls; addicts often self-inject harmful impurities, with disease-producing, potentially fatal consequences.

Basic and Clinical Research. NIDA funds most basic research on drugs of abuse. Its support already has led to a dramatic discovery that has altered general concepts about brain function. Since 1973, research has shown that the brain: 1) has highly specific receptors for such opiates as morphine and heroin and 2) makes and stores

substances called opioid peptides that have actions quite similar to those of morphine. Among many potential benefits, the elucidation of how these important neuroregulator systems work and what mechanisms control their activity may suggest ways to separate the actions needed for pain relief from those causing addiction. Such research could aid the fight against drug abuse by suggesting new treatment approaches and might lead to a new class of pain-relieving agents as effective as morphine but without addiction potential.

The opioid systems have ramifications for many aspects of human physiology and behavior, including regulation of respiration, blood pressure, appetite, and hormones; also, they may be involved in common mechanisms for various compulsive behaviors and "loss of control"; for reinforcement and pleasure or pain; and for the complex and intertwined phenomena of tolerance, dependence, and withdrawal. Discovery of the opioid peptides is an exemplar of the unexpected fruits of basic studies of brain function and has stimulated a vigorous search for other brain neuroregulators.

Two treatment programs for opiate addicts have emerged from the research findings--methadone maintenance and use of opiate antagonists. Adherents of the former approach endorse the use of a long-acting opiate to maintain tolerance and minimize the acute positive effects of a heroin injection; those favoring the latter prefer an antagonist to the opioid receptors, blocking any effects from opiate usage. More information is needed about each of these strategies, to determine their effectiveness, their relative advantages and risks, and their optimal use. Other potentially useful treatment approaches have yet to be tested extensively, including therapies that emphasize mainly behavioral or social change. Also, successful existing programs should be examined closely, to identify key elements that can be used to improve other types of interventions.

Researchers and clinicians increasingly question the value of dichotomizing drug dependency into physical and psychological components. For example, acute effects of a drug may differ greatly, depending on whether a user is taking it while alone or as part of a group activity. The role of social factors and learning in addiction and in treatment response is illustrated by research on soldiers who had been addicted in Vietnam, were detoxified there, and then returned to the United States. They had a much lower relapse rate than do addicts who leave their usual setting to withdraw in the different environment of a hospital and then return to the community where they are accustomed to abusing drugs. Some animal studies confirm that environment can be a key factor in drug addiction. Thus, animals tolerant to heroin in one setting may react as if they had never had heroin before, if they receive the same dosage of drug in a different room. In another interesting approach, animals taught to associate a ringing bell with receiving a heroin injection will have a full-blown withdrawal syndrome if they first hear the bell and then receive an opiate antagonist--even if they have been completely drug-free for months.

Such accumulating evidence has impelled investigators to go beyond explanations of these phenomena that invoke a single physiological or biochemical mechanism. A psychological theory known as opponent processes, which postulates that many behaviors and brain mechanisms entail a dynamic balance between two or more systems, is one intriguing perspective that researchers recently have begun to

apply to problems of drug abuse and addiction. It and other new viewpoints are potent stimulants for novel research in many parts of the biobehavioral sciences.

Other Drugs of Abuse. Opiate addiction is only one of the severe drug abuse problems in the United States. Other important drugs include such stimulants as cocaine and amphetamines; psychoactive substances such as LSD, dimethyl-tryptamine, and phencyclidine (PCP); various sedatives and minor tranquilizers, including barbiturates and benzodiazepines; and drugs used by broad segments of the population, including nicotine and marijuana.

Efforts to understand drug addiction must include careful study of both psychosocial and biological determinants. Societal norms help mold individual behavior, so information about the establishment, maintenance, and disintegration of norms may help to clarify aspects of drug abuse. Also needed are studies of the effects of drug use on social psychological processes, a type of research called sociopharmacology; such research may help illuminate the positive effects of drug use for the individual and the social groupings that promote and help maintain the behavior. The neurosciences must obtain more information about brain systems through which various drugs act, with an eye toward identifying common mechanisms of drug habituation and tolerance. As one illustration of the potential overlap of psychosocial and neuroscience research, it is interesting to note that psychological stress can change brain and blood concentrations of the opioid peptides--through mechanisms yet to be established.

Biological researchers are discovering important clues to mechanisms by which several of the drugs of abuse act. Many alter neurotransmitter formation, reuptake, or receptor function. For example, PCP markedly increases the activity of the brain dopamine system, producing what has been termed a "dopaminergic storm"; it also may act on a specific brain receptor, raising the possibility of a naturally occurring substance for which PCP is an agonist or antagonist. Discovering the mechanisms of action of such drugs could lead to improved treatments of acute toxicity, withdrawal symptoms, and dependence. An excellent example of such a result is the use in emergency rooms of naloxone (Narcan), a specific opiate receptor antagonist that can completely reverse the respiratory suppression and other adverse effects of an opiate overdose.

Psychosocial research is beginning to yield information needed about the incidence, use patterns, associated behavioral changes, and long-term mental and behavioral effects of drugs of abuse. Such data are vital in treatment and educational efforts. Epidemiological studies are essential to determine when during the life course people are most at risk of initiating drug use and to develop the basic information about those periods of life that can be used to improve targeted preventive interventions. Such projects should study both people at high risk of becoming drug users and those who seem unusually resistant to becoming drug abusers. Research on polydrug abusers also is needed. At least among people with personality disorders, using drugs at an early age and growing up in a disordered family seem to be risk factors of later polydrug use. Many experts believe that closely supervised residential settings can treat such people effectively, but this intervention has yet to be evaluated fully.

Alcoholism and Alcohol Abuse

Alcoholism and alcohol abuse is a major social problem and a serious disorder. Alcohol use is an integral part of American society. In this country and many others, alcohol and tobacco are unique among strongly habituating substances in being legally sanctioned for recreational use. A substantial fraction of the human race's energy and resources is devoted to producing and consuming alcohol--and to dealing with problems that its excessive use causes.

Clinical Syndrome. Alcoholics and alcohol abusers are frequent visitors to hospital emergency rooms who constitute a major, often hidden, healthcare cost. Nearly 100 million Americans drink alcoholic beverages, which greatly complicates efforts to assist the 10 percent of drinkers for whom alcohol use is a major impediment to physical and mental health and social functioning. Acute forms of alcohol-related difficulties range from the "blind drunk" condition of alcohol intoxication to the "DTs" of a full-blown alcohol abstinence syndrome. Each problem requires different treatment modalities, most of them symptomatic and empirically derived. As more is learned about biological substrates and psychosocial aspects of alcohol abuse and alcoholism, it may be possible to design more specific and rational interventions.

Alcoholics exist at every socioeconomic level and in essentially every subculture of American society, but with an uneven distribution. Historically, most alcoholics have been male, but the number of identified female alcoholics is on the rise in the United States. Alcoholism clusters in families, and it has strong heritable features in some alcoholics. Powerful, poorly understood cultural patterns mold the social uses of alcohol. An especially disturbing recent trend in this country is the evidence of increased alcohol use among teenagers.

A continuing problem for medical practitioners and researchers alike has been the diverse manifestations of alcohol abuse. The familiar "skidrow" alcoholic is only one form. Cultures and ethnic heritage influence both the rates of alcoholism and its presentation. Some alcoholics have a strong genetic predisposition to alcoholism, but many do not. Some people maintain good social, interpersonal, and legal function, despite episodic or continuous excessive alcohol intake; some indulge in bouts of heavy alcohol use between problem-free intervals; for others, excessive alcohol use is just one aspect of a broader pattern of self-destructive behavior. In recent years, experts in the field have begun to tackle the important task of distinguishing better among subtypes of alcoholism and alcohol abuse. Such efforts not only will help sharpen research questions about alcoholism and alcohol abuse but also should increase the specificity of prevention and treatment interventions.

Two problems associated with alcohol use are particularly troubling. The fetal-alcohol syndrome has been recognized only recently as a broad social concern. Its significance is enhanced by the need to protect the developing child, which may suffer life-long consequences. No problem in mental health better illustrates the importance of prevention, because the difficulties that the child experiences typically are untreatable. Furthermore, pregnancy may be a propitious time to make an intervention; research suggests that, if asked, many pregnant women who are

moderate alcohol users when not pregnant will abstain from alcohol to benefit the unborn child. A second clinical entity is the alcohol-violence syndrome, which can severely disrupt social relationships and may result in physical harm for people closest to the person using alcohol.

Basic and Clinical Research. In 1980, the IOM released a comprehensive report called Alcoholism and Alcohol Related Problems: Opportunities for Research, which included an extensive list of worthwhile directions for alcohol research. The Board endorses the recommendations and conclusions of that report and urges adequate funding for its implementation. Well-trained investigators already exist who could enter alcohol research; as needed, additional scientists can be trained. NIAAA's innovative uses of relatively meager research funds to attract talented investigators in the biobehavioral sciences to studies of alcohol-related problems are especially noteworthy; some could serve as useful models for enhancing research portfolios on other important topics within the ADAMHA mandate.

The effects of alcohol on neurobiological processes, especially on neurochemical mechanisms, remain largely uncharted. Alcohol alters many chemical processes in the brain, mainly through unknown mechanisms. Support of basic research that can add to the scant knowledge base now available about alcohol's potential sites of action is crucial. Some scientists have proposed that alcohol metabolites may affect neurotransmitter function indirectly by altering the effectiveness of communication between nerve cells; this potentially important action of alcohol has received little study. Alcohol also has potent direct effects on cell membranes. For example, it alters membrane fluidity, which may alter the function of the many proteins such as receptors and ion channels that modulate neuronal activity. Of great interest are differences and similarities among subtypes of alcohol abusers, for example, between people with a strong genetic component versus those without. The search for the biochemical underpinnings of alcoholism and alcohol abuse may have the same kind of widespread effects that NIDA's farsighted support of research leading to the discovery of opioid peptides had in opening new avenues for understanding brain function.

Much remains to be learned about the effects of alcohol on a variety of the brain's developmental and maintenance functions. As noted earlier, its impact on development is pervasive and costly to babies born with the fetal alcohol syndrome. Alcohol seems to impair regeneration and recovery from injury and to destroy nerve centers. Controlled clinical research settings are needed to monitor the effects of alcohol on a range of variables, from neuroregulator function to brain electrical activity. Such clinical research may yield pivotal insights into underlying mechanisms of the effects of alcohol on mood, behavior, attentional mechanisms, and sleep states.

Many questions about treating alcohol abuse remain unanswered. The only available drug treatment entails daily administration of disulfiram (Antabuse), a drug that induces violent physical reactions to alcohol. As is true for programs for opiate addicts, a minimum requirement for success is a strong, continuing commitment--not characteristic of many addicts. Some abstinence programs are successful with certain alcoholics. Characteristics of those programs and of people for whom they

are effective should be assessed, so that more people can be helped either with existing programs or with modifications of them. Special attention should be given to establishing more effective collaborations among professional treatment programs and self-help approaches such as Alcoholics Anonymous. The scant existing evidence is consistent with the possibility that self-help organizations work, at least in part, by providing an alternative social network based on the mutual bond of being an alcoholic. They have helped many alcoholics, and continued efforts are needed to study their methods systematically, to gain a clearer understanding of why they work and for whom, so that treatment programs can be structured accordingly.

Prevention of alcohol problems also needs further study. Far more information is needed about psychosocial aspects of alcohol use. Epidemiological data, for example, on evolving patterns of alcohol use by children, teenagers, and women, would be of great help for developing effective educational and psychosocial interventions. Alcohol use often begins in social settings, arguing for the value of learning more about its sociopharmacology, including how the social functions of alcohol use change over the life course. The effects of alcohol on perceptions of power and status also need more basic and applied research, especially with respect to the role of peer pressure in establishing patterns of alcohol use. Principles gleaned from peer programs for smoking prevention and from community-based cardiovascular disease risk-reduction programs may be especially informative.

Personality Disorders

Although many people have discrete episodes of an illness such as anxiety, depression, or schizophrenia, others have more chronic problems that often seem to result from their character style. When such personality traits become disruptive for the individual, the family, or the social environment, they are called a personality disorder. The signs and symptoms of two personality disorders are described below to illustrate this type of problem.

Little information is available about either the prevalence of personality disorders in the United States or their direct and indirect economic costs. However, it seems likely that people with antisocial personality disorder contribute largely to the current burden on the criminal justice system. Some relatively preliminary work on borderline personality disorder suggests that it occurs in 2 to 4 percent of the general population. People with this syndrome make disproportionate use of mental health care services; for example, some studies suggest that borderline personality disorder is a primary diagnosis for 10 to 20 percent of all psychiatric hospital inpatients. The prevalence of personality disorders among psychiatric outpatients and in medical patient populations is unknown but also may be large.

Clinical Syndrome. Adults with antisocial personality disorder have a long history of being unable to follow social conventions. Usually, problems begin by early adolescence. In school, they may have had poorer grades than expected for their intelligence, been truant repeatedly, and been expelled or suspended for misbehavior. At home, they are likely to have struggled constantly with their

parents, lied persistently, violated the rules, and run away repeatedly. Their peer relationships during that time will have been characterized by repeated fights, casual sexual relationships, frequent drunkenness or substance abuse, thefts, and vandalism. As adults, people with antisocial personality disorder remain unable to accept responsibility. They cannot hold a job for more than a few weeks or months; nor can they maintain an enduring, close emotional relationship, drifting from one sexual partner to another or from marriage to marriage. They may fail even as parents, letting their children suffer from malnutrition and inadequate medical care, as they squander money needed for such necessities on personal items. Other manifestations of recklessness and impulsivity are likely to include repeated failures to honor obligations such as debts, an inability to plan ahead, reckless driving, excessive use of drugs or alcohol, a pervasive unconcern for telling the truth, and a tendency to get into physical fights.

Borderline personality disorder also is characterized by impulsivity, usually manifested in a variety of potentially self-damaging behaviors such as shop-lifting and excesses in spending, sexual activity, gambling, drug use, and eating. In addition, people with this syndrome often deliberately hurt themselves physically, making suicidal gestures, cutting or burning themselves, or getting involved in accidents or physical fights. Typically, they have stormy interpersonal relationships, with frequent wide swings in attitude from excessive idealization to utter devaluation; they regularly manipulate those around them to achieve their own ends. Their emotions are intense and marked with inappropriate outbursts of anger and frequent shifts of mood, including periods of depression or anxiety. Often, such persons chronically feel empty and bored and cannot tolerate being alone. They may be wracked with worries about their identity, including concerns about self-image, sexual preference, long-term goals, friendship patterns, and values.

Treatment of severe personality disorders is problematic. Drug therapy usually is rather ineffective, although careful selection of patients who have affective or psychotic features may improve the response rate. Intensive, analytically oriented individual psychotherapy and some forms of group therapy appear to have somewhat better success as interventions for some of the severe personality disorders; but large, well-controlled studies of these approaches are lacking.

Basic and Clinical Research. Most research on personality disorders still is at the stage of defining the disorders more precisely and gathering information about their natural course. For example, the concept of the borderline personality has evolved substantially from initial hypotheses fifteen years ago that patients with this syndrome "bordered" on schizophrenia. Careful longitudinal studies of objectively defined patient populations have shown that most borderline patients do not later become schizophrenic. As a consequence of such outcome studies and of insights provided by psychoanalytic research on this population, many experts in the field now view the borderline syndrome as more closely related to the affective disorders.

Current diagnostic systems characterize disorders on the basis of observable or reportable behaviors or feelings that occur in a specified time, or episode. Personality disorders fit less well into such a scheme, because they are life-long,

often with a waxing and waning course. Much work is needed yet to separate the personality disorders into distinct, homogeneous subtypes and to define their overlap with other major mental illnesses. Such studies can form the foundation for research on the etiologies of these disorders and on more effective treatment and prevention interventions.

The search for causes of personality disorders again demonstrates the interdependence of specialties within the biobehavioral sciences. Using borderline personality disorder as an example, investigators have been drawn increasingly toward the hypothesis that the syndrome arises from a combination of biological vulnerability and early developmental trauma which prevents the individual from acquiring the ability to maintain a balanced concept of self and others as having both good and bad qualities. Except in extreme cases, neither insult alone may be enough to create the disorder; but the relative contribution of each probably differs among patients. Studies are needed of infants and young children that look in more detail at the ways in which concepts of self and others can fail to develop normally. Also important is research on how this syndrome appears in adolescence and whether detection and intervention at that age or even earlier can prevent later problems.

Personality disorders are notoriously difficult to treat, both because the patients often are refractory to available treatments and because they place huge strains on caregivers and treatment settings. Few general treatment principles have yet been identified. Thus, clinicians still argue heatedly about the merits of hospitalizing borderline patients. Some believe that even short-term hospitalization makes them worse and should be avoided at all costs; others think that long-term hospitalization in a highly structured milieu is a key to effective treatment. The appropriate role of drug treatments remains equally unsettled. Such controversies can only be resolved in careful clinical trials. Exploration of ways to help caregivers and treatment settings withstand the pressures that such patients create would be invaluable. Also needed are studies of how social networks can be utilized or created to provide long-term support for these patients outside the formal mental health care system.

Research Progress on Special Populations

Mental Disorders of Childhood and Adolescence

In a field with a series of overwhelming needs, childhood mental disorders remain noteworthy. As mentioned earlier, about 2 million children have such severe mental disorders that they require immediate care, and another 8 to 10 million need help but less urgently; yet, only 500,000 of them receive any kind of treatment through the mental health care system at present. By contrast, about 74 percent of the 7.6 million physically handicapped children in this country receive some sort of service.

Many adult problems have their origins in childhood. Childhood and adolescence are periods for learning coping skills, and the relative success in achieving such skills may have profound effects throughout life. Clearly, major stressors totally beyond a child's control can occur during that time, including separation, divorce, and economic dislocations. What remains to be elucidated are specific factors that determine the effects of such stressors for a given individual, whether those effects can be ameliorated with directed interventions, and how such interventions are best administered.

This section briefly surveys some of the range of severe childhood mental disorders that can benefit from a vigorous research effort. Major problems of this age group include: 1) developmental disorders of infancy, 2) hyperkinetic behavioral and attention deficit disorders, and 3) psychotic disorders in children. These disorders and the research questions they pose are discussed in the following materials because they are illustrative of this portion of the biobehavioral sciences. Yet the list is far from exhaustive. Among other serious problems are accidents, depression, developmental and coping failures, drug abuse, eating disorders, and the complex issues surrounding child abuse. Somatopsychic disorders are additional major causes of disability that merit vigorous study, along with psychological complications of such chronic childhood physical illnesses as ulcerative colitis, asthma, diabetes, and other metabolic diseases.

Frequently, childhood disorders are deviations from or arrests of usual development, so efforts to understand them thoroughly must include careful study of normal developmental processes and the biological, psychological, and social factors that impinge on those processes. At the very least, information about normal development can facilitate early detection of problems greatly. Stable support for longitudinal studies would enable investigators to examine aspects of environment, genetic make-up, child rearing, and other psychosocial and biological factors that contribute to adult health or dysfunction. Consortia of longitudinal studies could be established to minimize cost and maximize effectiveness.

Despite severe limitations in manpower and resources, research on childhood and adolescent disorders is progressing. Still, it trails far behind many other parts of the biobehavioral sciences. Some of the most severe problems undoubtedly result in large part from some dysfunction in the biological substrate of development and brain organization; others may arise mainly from psychosocial causes. Yet, perhaps even more than for adult diseases, these disorders usually must be viewed

from the broadest possible perspective, for they occur in the context of intimate, sometimes fragile interconnections among a child's constitutional endowment, mental development, physical health, and family and social environment.

Disorders of Infancy. The past decade has witnessed a marked expansion in knowledge about physiological, cognitive, emotional, and social aspects of infant development. Much creative work has led to discoveries such as the ability of very young infants to recognize and respond to visual, tactile, and auditory sensations; the existence of strong emotional ties between infants and their caregivers even in the early weeks and months of life; and the emergence during the first year of life of complex interactions between infants and their social environment as development proceeds.

Among other uses, normative data in areas like those just mentioned are helping researchers and clinicians to identify deviations. Thus, it is now possible to detect many regulatory and attachment disturbances as early as four to five months after birth. Such infants often will fail to habituate to routine levels of sensory stimulation, creating a pattern of hyperarousal. They may react to human contact as if it were aversive, shown by the way they arch the back; become rigid; hold their muscles in continuous extension; turn their head away from rather than toward caregivers; and maintain a solemn, unresponsive facial expression. Other infants, especially those with environmental deprivation, will display a pattern of hypoarousal, with poor muscle tone, failure to alert to the presentation of sensory stimuli, and sometimes failure to gain weight.

A new field is rising to meet the challenge to design better ways to detect and prevent developmental problems. A key area of interest in that context is further study of interactional processes. Technical and conceptual advances now enable investigators to quantitate many infant emotional and social patterns objectively. Such techniques help both in studying infants with diagnosable disturbances and in collecting data on normal and high-risk patterns. Identifying constraints on capacities for forming and maintaining bonds and relationships throughout the life course is a critical research need. Such research may be central to delineating how early experience can catalyze or inhibit the later development of behavioral disturbances.

A related line of inquiry involves studies of interrelationships among physiological, cognitive, emotional, and social development. Using new monitoring techniques, researchers can specify with reasonable precision the state of an infant's physiological and sensory processing systems and then can relate those capabilities to observable behaviors. Such research may pick up early physiological and behavioral risk factors and clarify their connection to infant disturbances and subsequent psychopathology in childhood. For example, by four months of age, infants with attachment disorders already fail to respond appropriately to usual human auditory, visual, tactile, and emotional stimuli. Ideally, these types of studies would include state-of-the-art assessments of at least: 1) neuroregulator metabolism, 2) autonomic nervous system function, 3) brain electrical activity, 4) information processing through each sensory pathway, 5) social and affective interactions, and 6) caregiver patterns that accentuate or diminish deviations.

In studying older children and adults, investigators find it hard to distinguish the self-perpetuating consequences of having the disturbance for a long time from early etiological factors or underlying mechanisms. Research on disturbances as they form would provide a new perspective for understanding basic mechanisms and should markedly enhance early diagnosis and prevention efforts. Such work already has helped generate several clinically oriented models of early interventions designed to prevent developmental, learning, and behavioral disorders. Recent applications of such models have yielded impressive decreases in the appearance of subsequent adverse outcomes in vulnerable children born into high-risk environments. Extensions of this type of research could determine the specific populations for which interventions are most likely to be effective and the generalizability of the interventions to various childhood disorders.

Hyperkinetic Behavior and Attention Deficit Disorders (HBAD). This collection of disorders has many names, with varying degrees of overlap: hyperactive child syndrome, hyperkinetic syndrome, brain damage syndrome, and minimal brain dysfunction. The key feature in attention deficit disorders is impulsiveness and distractibility, rather than excessive motor activity. The incidence of hyperkinetic disorders is difficult to assess, but males outnumber females. Unfortunately, as a result of the largely empirical methods by which the diagnoses are made at present, some children receive the label inappropriately. Accurate diagnosis and effective treatment of these childhood disorders might be a major preventive measure for adult mental health programs.

Children with attention deficit syndromes may receive both drug and psychosocial treatments. Since the 1960s, much interest has centered on central stimulants, especially amphetamine (Dexadrine) and methylphenidate (Ritalin). While taking such drugs, some children are less hyperactive and more tractable and have longer attention spans; school performance improves, and home tensions ease. Not surprisingly, both parents and schools may pressure physicians to prescribe these drugs for "problem" children. However, the drugs may have side effects; and their ability to alter the long-term prognosis remains unproven, even for children who have short-term benefits. Nearly all professionals agree that children with attention deficit disorder also can benefit from appropriate psychosocial interventions; these may include special educational programs with small, structured classes, support programs for parents and siblings, and individual psychotherapy.

A variety of efforts are being made to gain an understanding of the causes of the attention deficit disorders, including attempts to define more precisely who is affected and to identify neurophysiological concomitants of the behavioral problem. Researchers also continue to evaluate treatment issues, including limits to the use of central stimulants and more precise assessments of long-term outcomes. Questions about long-term effects of using stimulants with these children and ways of minimizing harmful side effects still must be answered.

A range of research to uncover the bases of attention deficit disorders needs support. Little is known about the mechanisms that control normal brain development and influence attention and concentration. Such basic information is essential for understanding disorders that manifest themselves as attention deficits.

It still is unclear which attention deficit disorders reflect brain defects and why certain stimulants can reverse some of the cognitive and behavioral deviations. To the extent that defects are biological, it will be necessary to study the genetic characteristics and explore neurochemical systems that are involved. Such work will demand increasingly precise diagnostic criteria for subtypes of attention deficit disorders; at present, it often is impossible even to distinguish children with neurologic dysfunction from those whose hyperactivity arises from anxiety, boredom, or depression.

Clarification also is needed of psychosocial aspects of the attention deficit disorders. Children with these problems are disruptive both at home and in educational settings. The consequences of such disruptions both for the children and for those around them have yet to be assessed adequately. It is likely that interactive patterns which quickly become established may help perpetuate or exacerbate undesirable behaviors. In this regard, research into more effective education of learning-disabled children is essential. Behavior modification and psychotherapy, whether as treatment modalities or as environmental shaping methods, may be fruitful research areas. Interdisciplinary programs are important and may lead to more precise information about optimal combinations of biological and environmental interventions, based on accurate assessments of behavioral symptoms of specific children.

Psychotic Disorders in Children. The childhood psychoses pose special problems. An especially distressing subset of these disorders, infantile autism, is characterized by development before age two-and-a-half years of the following: withdrawal, isolation, ritualistic activities, aloofness, language delays, and an intense dislike of change. These symptoms may be present at birth or develop progressively. Emotional contact and social relationships fail to develop. Such infants often fail to show expected "molding" behavior when held. They may lie in the crib, motionless and silent; gaze fixedly into space; or play with their fingers for hours. Another form of psychosis in this age group is childhood schizophrenia. Some such children display typical symptoms of adult psychosis as early as seven years of age, but many have thought disorders unique to childhood.

Distressingly little can be done about childhood psychoses. There is general agreement that most involve some sort of biological brain dysfunction, but psychosocial factors can affect their course. Research on intrinsic brain dysfunctions ultimately may identify the biobehavioral mechanisms involved and thereby suggest routes for devising more effective treatment and prevention interventions. Needed investigations include establishing normative data about the anatomical, biochemical, and neurophysiological development of the brain; such work lags far behind other types of basic brain research. Also, interactions of biological processes with normal psychological and social growth and development must be better understood. Of great importance is the search for good animal models. Genetic and anatomical studies of brain dysfunction can go forward more quickly and safely in animals than in human beings, and animal models facilitate trials of new drugs and studies of their actions.

Strikingly little research has been done on neuroregulator function in childhood psychosis--in marked contrast to the productive work done on adult schizophrenia and depression. Recent work strongly suggests that some autistic children have elevated concentrations of serotonin in blood, and preliminary studies suggest that fenfluramine, a drug that blocks the actions of serotonin, reduces symptoms in some autistic children. Also of interest is preliminary evidence that some autistic children develop antibodies against serotonin receptors. Such research gives impetus to further study of serotonin and other neuroregulators. Studies should include a full survey of neuroregulator mechanisms, looking for disorders of synthesis, release, degradation, receptor function, or activity imbalances among several neuroregulator systems that function in parallel.

Clinical work is needed at many levels including the development of better diagnostic tools, studies of the relationship of childhood psychoses to adult forms, and exploration of possible genetic contributions. Basic research on developmental processes may yield data that are needed to clarify changes that occur with severe disorders. Cognitive psychology, ethology, sociology, and other behavioral sciences also can contribute, for example, by rigorously testing suggestions that some behaviors which characterize autism may be adaptive, in the sense that they partially compensate for an underlying disorder. Thus, some experts have noted that many of the behaviors effectively decrease environmental inputs, perhaps protecting an easily overloaded sensory input system.

The search for better treatments must continue. No available drugs are as effective for childhood psychoses as are antipsychotics for adult psychoses. For the childhood psychoses, antipsychotic drugs help control behavior but lack the specific therapeutic actions they have on adult schizophrenics. A number of intriguing clues suggest promising lines of research, but few investigators are available to pursue them. Only the combined efforts of basic scientists and clinicians can be expected to produce the interventions needed to control the psychotic and other dysfunctional symptoms of childhood psychoses and facilitate the ability of these children to learn and to function in society.

Mental Disorders of the Elderly

For many reasons, including improved sanitation and more effective prevention and treatment of most infectious diseases, both the number and the proportion of elderly people in the United States has increased extraordinarily. Between 1900 and 1977, the contribution of elderly to the total population rose from 4 to 11 percent; by the year 2030, there will be more than 30 million persons over 65 and more than 13 million over 75. Yet, most health research has been on young and middle-aged adults. Of most direct relevance to this report, much of the existing information about brain function, behavior, and mental and addictive disorders may not apply to older adults, because a number of physiological changes in brain function accompany the aging process and because dramatic psychosocial changes have occurred in this country over the past several decades.

Because of its overall concern with brain development and function, ADAMHA appropriately supports some studies of the effects of aging on the brain. Other

federal agencies with major interests in aging and in the brain are the National Institute on Aging (NIA) and National Institute on Neurological and Communicative Disorders and Stroke (NINCDS). NIMH and NINCDS interests overlap especially in dementia research. Although both institutes support work on biological factors that contribute to the onset and progression of the dementias, their respective projects usually have quite different perspectives. Typically, such areas of overlap have enriched research efforts, not created redundancy; still, mechanisms are needed to encourage the various institutes to coordinate their programs in such large areas of mutual concern.

Dementias. Dementias are a widespread problem in the United States that will continue to increase, with the demographic changes already described. Their prevalence rises from 3 percent for people at age 65 to over 20 percent for those 80 years of age and older. At present, almost 3 million people 65 years and older, mostly women, suffer from a dementia. The current costs to society are at least \$12 billion annually, and they can be expected to rise rapidly in the coming years.

One major form of dementia, Alzheimer's disease, is illustrative of the devastating impact dementias can have. Lasting 2 to 20 years, its victims become unable to care for themselves or communicate their needs; they become incontinent, incapacitated, and totally dependent on others, whom they often treat with fear and suspicion. There is no known prevention or treatment. In fact, improvements in health care actually have increased the overall burden: more people survive to the high-risk age ranges; and afflicted individuals live longer, so they have time to deteriorate further.

Developing an understanding of the neurobiological causes of the dementias is vital. To date, it still is unclear whether the dementias represent an acceleration or worsening of the cognitive decline characteristic of old age or differ fundamentally from it, although a variety of data suggest the latter. One useful outcome of the needed basic research would be more detailed information about the cognitive decline that often occurs with age. Such knowledge could enable clinicians to detect changes that are associated with specific forms of dementia and, possibly, to devise treatments to correct or compensate for underlying causes.

Particularly important are basic science studies of changes in brain neurochemistry and neuroanatomy through the life course, which also are essential in other research on mental illness and addictive states. Basic scientists have made striking progress in perfecting ways to map pathways of particular neuroregulator systems and to identify enzymes and other markers of cell function with light and electron microscopy. Such techniques already have been applied to looking at brain changes that occur in Alzheimer type dementia, showing some decreases in acetylcholine and norepinephrine-containing neurons.

Improvements in diagnosing and treating dementias are needed badly. Some people who appear to be demented actually are severely demoralized or depressed; some may be having adverse reactions to medications such as sedative-hypnotics. If diagnosed appropriately, such individuals are likely to respond to suitable

psychosocial and drug interventions, with improved intellectual performance that enhances their lives and materially reduces the need for costly hospitalization or other forms of special care. New noninvasive measures of brain structure and activity, described earlier, may be especially useful in this regard. Neurophysiological tests of psychological and physical performance that can delineate areas of poor brain function also are vital both for advancing basic research and for clinical applications.

The etiology of Alzheimer type dementia still is obscure; it may involve biochemical changes through genetic mechanisms or environmental agents such as a virus or environmental toxin. An immunological cause also is possible, and studies of psychoimmunology are a useful thrust for future research. Studies of chromosomal defects are under way, and these and other potential genetic contributions to the disorder should be assessed, including possible defects in neuronal cell migration. Fortunately, improved treatments may emerge even as the search for specific causes continues. For example, Parkinson's disease, a movement disorder, often may arise from a viral infection; yet its treatment is based on increasing the activity of the dopamine neurotransmitter system.

Much research also is needed on the psychosocial aspects of dementia, for example, devising better methods of testing and subtyping patient populations in terms of severity and type of illness. Also of value would be improved tests of function such as measures of the ability to reason and make logical judgments. Such assessments must address both verbal and nonverbal skills, because dementias often deprive people of intelligible speech; they also must compensate for concomitant changes occurring with normal aging. In terms of developmental processes and changes, longitudinal studies are needed to find ways of detecting people at risk for developing dementia.

Psychosocial research is important for devising optimal ways to care for those with dementia, both within and outside the family. Little is known about the differing ways people from various socioeconomic and cultural backgrounds perceive dementia in themselves or other family members and how those perceptions affect the optimal form of care. For a number of demented individuals, the family constitutes the fundamental support system, often at the expense of substantial disruption of normal family functioning, with unwanted effects on everyone involved. Confinement, conflicts, low life satisfaction, and feelings of being a burden or being burdened can strain relationships severely. If the strains go unheeded, tensions may result in "burn-out," and the caregiver also may begin to have health problems. Development of psychosocial interventions to aid caregivers and patients is essential. Systematic work is needed in this sparsely studied area to build on basic studies of family and group processes. Basic and theoretical studies also require support, for most research on family and group processes has focused on the first half of life; many of those observations probably do not apply to the problems of caring for an aged, demented family member.

Other Disorders in the Elderly. Depression was discussed earlier and receives little additional attention here, except to repeat that sometimes elderly people have a depression that is ignored or undiagnosed. Careful attention must be given to ways

in which depression manifests itself in this age group. More information is needed about the role of psychosocial stressors in increasing an elderly person's vulnerability to depression. Elderly people, who often have diminished physical and mental reserves, may face especially strong stressors, including illness and the adverse changes that typically accompany growing old such as loss of loved ones, forced relocation, and increased dependence on others. The ability of psychosocial and drug interventions to counteract deleterious effects of such changes deserves further study.

Little is known about the usual changes that occur in such social processes as status, normative behavior, affiliative behavior, and conformity through the life course. Ultimately, such information may prove helpful in work with the normal aged as well as with those who have various forms of illness. Studies of the effects of nursing home care may be of special value. For example, research suggests that homes providing unnecessary services promote feelings of dependence which may have adverse effects on the clients' health; elderly people who maintain their independence as much as possible and who view themselves as being involved in meaningful tasks may function more effectively, have lower rates of illness, and live longer. However, programs must be sensitive and sensible. For someone whose reserves already are taxed by illness, overemphasis of the need for independence and self-help may be so stressful that problems worsen, rather than improve.

Also important is the issue of alcoholism and alcohol abuse in the elderly, which, in the United States, affects about 8 percent of those over 65 years of age. As with depression, research on alcoholism in the elderly probably can use some of the existing data on younger populations; but there may be large differences for elderly people in such realms as what makes them drink, how potent the effects of alcohol are on brain and other bodily functions, and how people who become alcoholics in old age can be helped to stop.

The Chronic Mentally Disabled

Chronic aspects of mental illness and addictions are extremely important for society. As knowledge about and treatments for these disorders has improved, those interested in care of the mentally ill and addicted have become increasingly concerned about the large number of chronic, untreatable ill. Some chronic forms of depression, psychosis, anxiety, and addiction simply are not amenable to existing interventions. Chronic mental illness imposes enormous drains on community resources for health care, social services, and economic aid. Chronic abuse of various drugs exacts penalties that range from serious physical illness to changes in behavior, including criminality.

Patients with chronic mental illness who require prolonged hospitalization cost taxpayers tens of thousands of dollars a year, but outpatients also create substantial expense. Widespread policies that have encouraged deinstitutionalization of patients have created new problems. For some, deinstitutionalization may be appropriate; for others, it is not. The level of care and resources available outside of hospitals have proven to be inadequate for many former inpatients; throughout the United States, a number of chronic mentally ill individuals no longer have access to a

working system of mental health care. It is increasingly clear that this problem will not yield to a single, broad strategy such as state mental hospitals or community-based outpatient programs. Although solutions are not readily apparent, research is one key.

Biological research is progressing for each of the severe disorders with which ADAMHA is concerned, as described throughout this report. More information is needed about biological aspects of the causes of these disorders and about treatment, particularly chronic treatment. Studies should examine the natural histories of these disorders and evaluate the long-term effects of chronic treatment within that context, both for the afflicted individuals and for their offspring. Also needed is basic research on developmental processes and the ways in which commonly used drugs can affect them. For disorders that may require prolonged or even life-long treatment, clinicians need more effective and safer drugs to offer their patients.

Psychosocial research is extremely important in the attack on chronic disability. Using existing survey technology, it should be possible to begin the crucial process of defining which disorders contribute to the population with chronic mental illness and identifying what leads to a chronic course in some but not in others. The social sciences can add to knowledge about relationships between environmental circumstances and disease outcome. Evidence already suggests that some supportive social and family environments are helpful for certain types of patients, but more must be learned about what types of support are most appropriate for which disorder. Also, the sometimes crushing burden that someone with a chronic mental disorder places on the family must be examined in more detail, to discover how that load can be eased.

Research on living arrangements for chronically disabled people outside the home, including such options as half-way houses, could yield more information about factors that lead to success. For some, such facilities are far more humane treatment settings than is institutionalization. The social and psychological sciences, for example, social ecology, will be useful for making guidelines about the best combinations of psychiatric hospitals and nonhospital psychiatric care centers and for defining criteria to match the patient with the optimal treatment setting. They also can help to clarify issues about the homeless mentally ill, who are an increasingly common sight on the streets of many major cities throughout the United States. Many of these people have never come to the attention of the mental health care system, despite severe mental disorders. Ways must be found to identify those who need care and to bring them into contact with appropriate caregivers.

Behavior and Health

In the past 30 years, prevention and cure of most infectious diseases has shifted the major causes of morbidity and mortality, so that chronic diseases now are the main contributors to the burden of illness in the United States and other developed countries. Behavioral factors are crucial in the development or management of such disorders or conditions as diabetes, cardiovascular disease, hypertension, obesity, and some types of cancer. Federal government statisticians have estimated that 50

percent of the mortality from the ten leading causes of death in the United States is attributable to aspects of life style. This suggests the great value of learning more precisely how behavioral factors affect therapeutic and preventive efforts across a wide range of diseases and disabilities. In 1982, the IOM published Health and Behavior, a superb review of this area that makes a number of sound recommendations. The Board strongly endorses the findings of that report.

Some types of behavior are risk factors of disease. Probably the best known behavioral risk factor is cigarette smoking, which is associated with an increased likelihood of a number of major illnesses, including lung cancer, emphysema, and heart disease. The 1984 IOM report Bereavement: Reactions, Consequences, and Care describes important research and treatment issues for a familiar psychosocial risk factor. Other known behavioral risk factors include excessive alcohol consumption, illicit drug use, insufficient exercise, diets with excessive calories or salt, nonadherence to sound medical treatments, and maladaptive reactions to stress or social pressures. A relatively new area of research interest with potentially far-reaching implications to health is that of the effects of disrupting the body's natural biological and psychological rhythms, as now happens to more than 25 percent of American workers who routinely change their work shift from day to evening or night.

For the leading causes of death in the United States, behavioral factors play an important role for a substantial number of the most common disorders: heart and vascular diseases, cancers, accidents, homicide and suicide, diabetes mellitus, cirrhosis of the liver, and lung diseases. The costs of morbidity are also large. More than one third of Americans who report that they are unable to pursue their major activity because of poor health attribute their disability to hypertension, heart conditions, or diabetes--all of which have heavy behavioral components.

Two key questions are whether behavioral risk factors of disease can be changed and if so, whether such a change is health promoting. Based on accumulating evidence from independent sources, the answer to both these questions is yes for "healthful" changes relating to several disorders. Thus, deaths from coronary heart disease declined by 20 percent during the 1970s--a decrease almost certainly linked in part to changes in smoking, diet, and control of hypertension. It also is clear now that many people find it hard to change their lifestyle, even in the face of known risks to health. Therefore, it is not enough to identify behavioral risk factors and show that changing them reduces the risk of disease; also needed are practical and cost-effective ways to help large numbers of people give up or never start behaviors that can have adverse health effects.

Basic and Clinical Research. Most studies of behavior and health are intrinsically cross-disciplinary, and many could appropriately involve collaborative efforts of ADAMHA with institutes in NIH. The work entails: 1) identifying behavioral risk factors and looking for underlying linkages between those factors and specific diseases; 2) studying how specific behaviors and attitudes enhance or hinder treatment, especially for such chronic illnesses as diabetes or hypertension; 3) developing better aids for people who want to change behaviors or give up habits that adversely affect their health; and 4) learning how social structures such as the

media or the workplace affect the health of individuals in the society, and whether it is possible and desirable to alter such influences deliberately and systematically.

Examples abound of needed research on various behavioral risk factors. Cigarette smoking may be especially apt, because it has received so much attention. Cigarette smoking is a potent habit; some experts in the field urge that it be called an addiction, mainly because of the astonishing difficulty the great majority of smokers have giving it up. Studies indicate that about 85 percent of people who sample more than a few cigarettes become regular users. Of those who later try to stop smoking, only one third are able to quit on their own for more than six months; most of the rest stay quit only for a few days, at best. Other experts demur, noting that smokers do not become tolerant to cigarettes or exhibit a true withdrawal syndrome when they quit. Some fear that labeling smoking as an addiction may be counterproductive, because it gives smokers a powerful rationalization for continuing to smoke. Full consideration of the advantages and disadvantages of calling cigarette smoking an addiction is beyond the scope of this document; but, the decision merits close scrutiny by policy makers and scientists in the field.

Smoking is one habit that nearly everyone agrees is undesirable, and its effects account for billions in health care costs. Despite this, factors that support the adoption and maintenance of this habit and hinder efforts to quit it still are largely unknown and unstudied. A concerted effort across several disciplines is needed to uncover pharmacological, physiological, neurochemical, behavioral, psychological, and social influences that contribute to the overall phenomenon of regular smoking. Such projects seem ideally suited for joint support across federal institutes. NIMH, NIDA, and NIAAA have expertise on addictions, habitual behaviors, and brain function; NHLBI has experience with large-scale prevention programs; NCI has knowledge about carcinogenic effects of substances found in cigarette smoke; and other NIH institutes also might find areas of overlapping interest. Collaborative ventures among institutes are rare, especially between components of ADAMHA and NIH. Although recognizing the organizational complexities of such joint efforts, the Board believes that they could be tremendously fruitful in selected cases, like the problem of cigarette smoking.

In another area, the effects of stress on health remains an important research focus. In 1982, the IOM released Stress and Human Health, an extensive review of this topic which concluded that stress clearly can have important effects on health and documented a range of evidence implicating stress as a risk factor for a large number of disorders. The study also emphasized how little still is known about the complex interactions that lead from physically or psychologically stressful events to health problems and other adverse consequences. For example, researchers have only begun to explore and characterize pathways through which stress can affect different parts of the body such as the vitally important cardiovascular and immune systems.

Stress and Human Health thoughtfully examined some key conceptual and methodological problems in a field characterized by research of markedly uneven quality; it offered a range of research recommendations. Among its major conclusions were: 1) stressors must be distinguished from the reactions they may produce and the health consequences that can result from those reactions;

2) reactions and consequences result from an interaction between the stressor and modifying influences that the individual and the setting impose; and 3) reactions and consequences often may be understood best from a life-course perspective. The report also opposed the common tendency to view stressors as "bad"; it emphasized that only consequences can be qualified as desirable or undesirable and suggested that frequent failures to make this distinction have created much confusion within the field. The issue of stress and health is intertwined inextricably with questions about health and behavior more generally, because behaviors of interest in the latter context often are stressful. The main focus should be elucidation of the link between the brain and the rest of the body.

Chronic disorders such as emphysema, diabetes, and hypertension are pertinent examples of the relevance of behavior to treatment, even when drugs are the primary form of therapy. Specific treatments are most useful when patients recognize the need for them and adhere to the regimen. For some disorders, patients may need to monitor a variety of physical signs and symptoms, as well as take medication correctly and reliably for a long time. An understanding of psychological and social factors that influence attitudes about being ill, seeking help, and deciding whether medical advice is trustworthy would be of value for creating interventions that improve the initial response and decrease subsequent relapses or progression of the disease.

Childhood and adolescence should be major areas of concern in studies of behavior and health. Lifelong benefits can accrue from such modest preventive efforts as neonatal metabolic screening and routine immunization. Now, efforts are needed not only to improve screening techniques and develop additional vaccines but also to engage parents and communities in widespread and consistent programs of disease prevention and health promotion. The knowledge base for such programs has begun to evolve, and in some areas it is ready for application. A recent and highly promising example is the incorporation of knowledge about adolescent exploratory behavior and peer relations into peer-guided programs to prevent teenage smoking and drug abuse.

Much remains to be learned about how best to help someone wanting to make long-lasting changes in a specific behavior. Smoking and consuming too many calories are two excellent examples of behaviors that many people in the United States want to stop but cannot. One innovative approach to this type of research that needs encouragement is the study of those who do succeed in changing their behavior without formal interventions. A detailed analysis of factors that fostered their success may suggest ways to facilitate changes in others.

Attention also needs to be given to societal issues of behavior and health, including priorities in the health care system. For example, some research indicates that a reduction of behavioral risk factors and identification and treatment of alcoholism and mental disorders can markedly decrease subsequent use of medical care resources of all types. This suggests the need to examine the effect on overall costs and care delivery of integrating mental health care and a preventive orientation into routine health care.

Careful study of the effects of social disadvantage on health-related behaviors also is important; such research may suggest ways of targeting interventions for populations who are at especially high risk for a particular disorder such as hypertension.

All of these examples tend to cut across traditional research and clinical fields, emphasizing the need for increased collaboration among the institutes, so that expertise within ADAMHA on behavior and brain function can be applied rapidly to the perplexing problems that remain about current major causes of the burden of illness in the United States.

Current and Potential Benefits of Research to Society

Basic and disease-oriented research can be expensive; yet, history has shown that the lack of research can cost much more. For example, the development and vigorous dissemination of the Salk vaccine for polio saved \$6 billion in the first six years alone. The total research investment of \$40 million from 1938 to 1962 is miniscule in comparison. Analogous considerations apply to the mental and addictive disorders.

The discovery of effective drug treatments for schizophrenia, mania, and depression in the 1950s markedly changed care of the mentally ill. For example, widespread use of drugs described earlier helped reverse the trend of rising populations in psychiatric hospitals in the United States. In 1955, the census peaked at over 500,000; by 1973, it was half that. After declining slowly for several more years, the number of hospitalized mental patients has stabilized, despite a growing general population and rising mental hospital admission rates. Antidepressant, antimanic, and antipsychotic drugs have been invaluable for treating patients before they need hospitalization and for helping to quickly return hospitalized patients to productive roles in the community. Psychological and social interventions also have helped to reduce the steady deterioration so long linked to severe mental disorders.

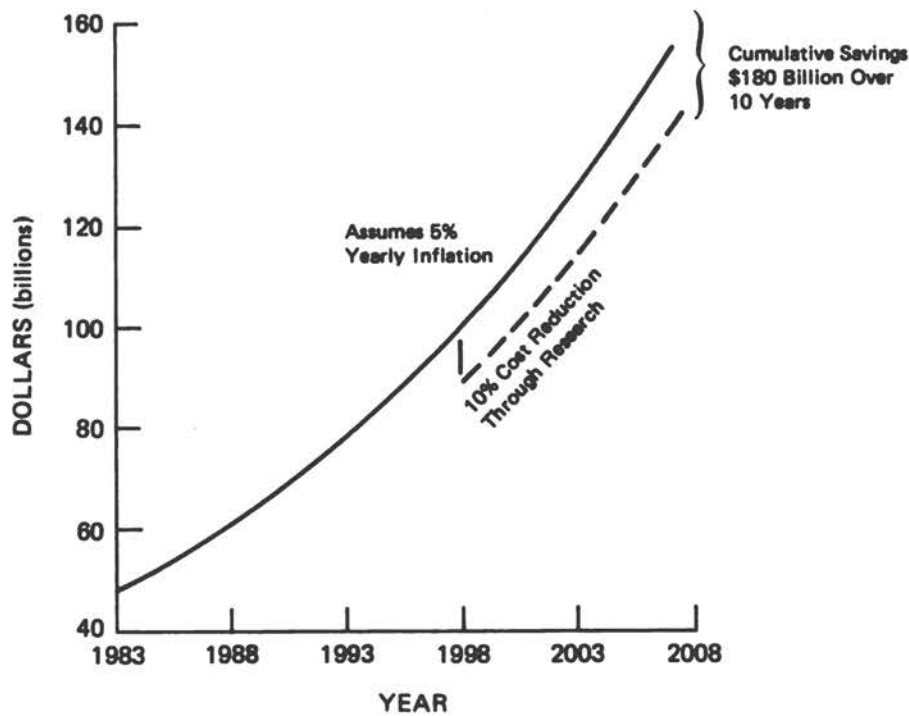
The substantial savings produced by the introduction of lithium salts to treat bipolar affective disorder are well documented. An Australian psychiatrist, Dr. John Cade, first noted lithium's antimanic effects in 1949; yet, it was not used widely in the United States until 1969. The NIMH was instrumental in facilitating its introduction into this country by funding careful clinical trials that demonstrated its efficacy and relative safety. Estimates suggest that, to date, lithium has produced cumulative direct and indirect savings of \$6.5 billion in 1969 dollars--or over \$17 billion of savings in 1983 spending power. These calculations used uniformly conservative estimates of the number of people who benefit from the drug and of the savings arising from its appropriate use. For example, they did not adjust for the country's increasing population, which adds to the number of people at risk of developing bipolar affective disorder. Thus, savings from lithium alone far exceed the total federal investment in research on mental disorders and addictive states, which has been substantially less than \$3 billion from 1948 to the present.

Major improvements in preventing and curing mental and addictive disorders still are needed. Many individuals remain disabled, often because available treatments do not work for them. Existing interventions for mental disorders and addictions typically are not curative, so even those patients who respond may relapse repeatedly, especially if adverse side effects discourage them from continuing treatment. The long-term goal is for definitive cure or prevention of such disabling disorders as recurrent depression, schizophrenia, childhood psychoses, and alcoholism; but even small steps toward that goal would produce large savings. For instance, direct and indirect expenses of schizophrenia in 1983 were an estimated \$48 billion; even at a conservative 5 percent annual inflation rate, those costs escalate rapidly. If research yielded an intervention that reduced costs even by 10 percent annually, its introduction in 1995 could save a total of \$180 billion by 2005 (Figure 1). Any one of several promising research leads might produce such savings, including

discovery of subtypes of schizophrenia that respond to novel drugs or development of a psychosocial approach that minimizes adverse reactions to stressors and thereby prolongs remissions. A broad research thrust is needed precisely because it is impossible to predict in advance where the breakthrough will be.

Psychological and social interventions typically have not enjoyed the dramatic results of drug therapies, but their role is becoming clearer. With respect to disorders exclusively within the ADAMHA mandate, some forms of psychotherapy appear to be as effective as antidepressants for treating at least some depressions. Also, studies have shown that people with schizophrenia can function better, stay out of a hospital longer, and require less medication if they are in the right kind of social setting. In addition some psychosocial interventions during infancy and early

FIGURE I
ANNUAL COST OF SCHIZOPHRENIA



Used with permission, from Wyatt, R.J. Science and Psychiatry. IN: Comprehensive Textbook of Psychiatry, Fourth Ed. (Kaplan, H.T., and Sadock, B.J., Eds.) Baltimore: Williams and Wilkins, in press.

childhood have proven to be efficacious and cost-effective in preventing severe developmental, learning, and behavioral disorders in vulnerable children, especially those in high-risk environments.

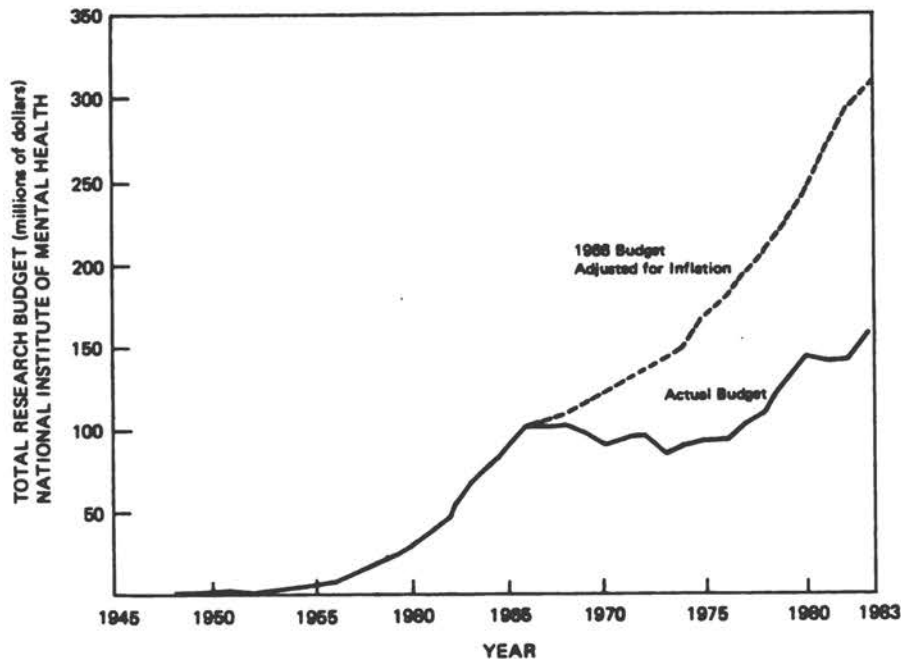
A developing knowledge base in psychology and social science also is cogent to unhealthful behaviors associated with physical disorders. For example, information about the origins of adolescent risk-taking behavior has been central to the recent development of relatively effective smoking prevention campaigns. Similarly, social learning theory has been applied to cardiovascular disease programs to create effective, low-cost community interventions that help people become aware of poor health habits and show them ways to replace those habits with more health-promoting ones. Even these few illustrations clearly document the potentially major role that basic advances in the psychosocial sciences can play in molding future treatment and prevention interventions.

The Present Level of Research Funding

The real purchasing power of funding for research on mental illnesses and addictions has declined sharply since 1966. This reduction occurred despite a burgeoning knowledge base about brain function and behavior of direct relevance to efforts to elucidate the causes of mental and addictive disorders. The disparity between research opportunities and funding has been widening for two decades, so the erosion cannot be ascribed to any single administration or session of Congress. Whatever its cause, the consequence is that Federal support of such work, residing mainly in ADAMHA, lacks the flexibility to foster the range of basic research needed to extend the knowledge base and also support applied studies to translate such information into improved prevention and treatment interventions.

Being the oldest and largest ADAMHA institute, the NIMH offers a good illustration of the funding problem. Figure 2 shows actual and constant-dollar research budgets for NIMH from 1948 to 1984. After rising steadily during the 50s and early 60s, the budget was unchanged or decreased from 1967 to 1977, as

FIGURE 2
NIMH RESEARCH FUNDING, 1948-1983



Yearly research budgets were provided by the NIMH. The correction for inflation is based on the Biomedical Research and Development Price Index.

inflation almost halved the real purchasing power. The Biomedical Research and Development Price Index is a federal measure of inflation for major costs in research; using a 1979 base, the index increased from 46.1 in 1967 to 86.0 in 1977; the NIMH budget was \$103.8 million and \$104.1 million, respectively. At no time since 1966 has an increase greatly exceeded the inflation rate.

Striking as these numbers are, they tell only part of the story: the potential uses for such funding also have increased markedly. As an example, in 1971, the Society of Neurosciences was a fledgling organization with only 250 members; today, it has over 8,000 members, many looking to the NIMH for funding. The Board examined support of this widely acclaimed area of research by reviewing the grants funded by the NIMH Neurobiology Section for fiscal 1982. That year, the Neurobiology Section budget was just under \$5 million for direct research costs. This amount, used to fund 55 grants in the entire nation, was all that could be diverted from other worthy NIMH programs to support the diverse and exciting work on such issues as basic mechanisms of neuroregulation, neuroscience applications of molecular biology, studies of the functional neuroanatomy of the brain, and the interface between basic neuroscience and clinical studies of major mental disorders. Although there may be minor sources of support for this field in other NIMH sections, the total number of grants and the total amount of funds clearly are woefully small. The quality of funded work was extremely high, but support simply was unavailable for many equally deserving studies. Some types of research such as program grants and innovative multidisciplinary efforts were especially rare, because the large-scale, long-term funding they require would deplete meager available resources. No internal budgeting maneuvers can address such shortcomings adequately, for each ADAMHA institute faces comparable funding problems for meritorious work in biological, psychological, and social sciences.

Effects of the major drop in real ADAMHA funding for research are hard to quantify, because many relate to lost opportunities and delays in progress. However, one concrete effect is readily demonstrable; NIMH now supports fewer research trainees than at any time since 1963. This is in the face of clear needs for researchers in a number of areas within the biobehavioral sciences, including, for example, fields relevant to the childhood disorders. Equally concerning is the diminishing support for young investigators. In 1977, over 25 percent of all NIMH research grants went to applicants under 36 years old; that proportion has fallen steadily and was 15 percent in 1983. The decline means that young scientists find it increasingly difficult to compete with more experienced researchers for rapidly shrinking resources. If uncorrected, this worrisome trend could leave the field without an adequate source of talented scientists in years to come. Yet, funding for established investigators already is markedly reduced, and many able researchers cannot obtain funding. Furthermore, even the grants that are awarded often are reduced administratively, to permit funding of as many deserving proposals as possible. It would be unwise to obtain funds for young researchers by further vitiating programs of more established scientists who are doing good work.

Conclusions

Evidence summarized in this report documents the major contributions of mental disorders, alcoholism, and drug abuse to the current burden of illness in the United States and attests to the progress already made in treating people with the most severe mental and addictive disorders. Yet, available drug and psychosocial treatments cannot help many of those with the most severe mental illnesses, and better interventions also are needed for alcoholism and other drug addictions. In addition, basic groundwork still is being laid for discovering ways to cure or prevent these disorders.

This section of the report presents some broad conclusions about the field and makes some specific observations about ADAMHA research programs. These are coupled closely with a call for a marked increase in research allocations, which the Board believes is crucial both for fulfilling the exciting promises within the field and for resolving many of the pressing problems that inadequate funding has created.

The Board notes that the 1980 Institute of Medicine report Alcoholism and Related Problems: Opportunities for Research concluded that "alcohol research is not funded at a level commensurate with the economic costs it imposes on society or at a level comparable to research funding for other major disorders" (p. 7). In 1982, another IOM committee surveyed the appropriate role of the biobehavioral sciences in addressing mental illness, alcohol-related disorders, drug abuse, and other health and safety concerns with behavioral origins. Based on its thorough review of the issue, that group asserted that, "Altogether, there is at present a remarkable discrepancy between unprecedented scientific opportunities on the one hand and diminishing support for such research on the other." (Health and Behavior: Frontiers of Research in the Biobehavioral Sciences, p. 319). In 1984, this Board draws similar conclusions.

To the extent that the lag in funding for research on mental disorders and addictive states may have been based partly on a belief that scientifically productive and clinically important research opportunities were meager in comparison to more traditional biomedical fields, that view now is totally outmoded. Given the manifold research needs and opportunities--a sampling of which is offered in this brief report--the Board recommends a prompt and substantial increment of research funding, so that the level of scientific effort in these areas begins to approach that deemed appropriate for other problems that contribute comparably to the burden of illness in the United States, for example, heart disease and cancer.

Areas of Progress and Promise

A tendency of those in the field to focus on what still remains to be learned should not detract from the impressive progress to date (Table 3). Substantial breakthroughs in understanding and treating major mental disorders and addictions seem likely in the foreseeable future. The rapidity with which basic biological principles of brain function are emerging far exceeds even the most optimistic predictions of two decades ago. Psychological and social science disciplines within the biobehavioral sciences are, perhaps, not as sophisticated with either their techno-

TABLE 3

MAJOR BASIC AND CLINICAL ADVANCES IN AREAS UNDER THE MANDATE
OF THE ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

- o Detailed information about brain chemistry, physiology, and structure has expanded markedly, as have the availability of sensitive, specific tools for monitoring brain activity, and conceptual models of neuronal and brain function.
 - o Methods of studying individual and group behaviors in animals and in human beings are becoming increasingly quantitative and sophisticated, and theoretical formulations are emerging of general rules to explain and predict such behaviors; these have exciting implications for future research and for a wide range of prevention and treatment strategies.
 - o Advances in individual biobehavioral disciplines make it increasingly feasible to study links between normal or pathological behaviors and specific aspects of brain function.
 - o Applications of basic knowledge to the prevention and treatment of mental illnesses and addictive disorders already have begun and are likely to continue at an accelerating pace over the next few years.
 - o Investigators are starting to inquire beyond disorders that afflict mainly young and middle-aged adults into the problems of populations with special needs, including children and adolescents, the elderly, and the chronic mentally ill.
 - o Compelling evidence suggests that the biobehavioral sciences have an appropriate role that extends far beyond concerns about mental and addictive disorders into the broader arena of interactions between behavior and health.
-

logy or their conceptual frameworks as are the neurosciences; yet, they already have shown their utility both for devising new treatments for some kinds of disorders and for facilitating the complex task of helping people make lasting behavioral changes that can improve their physical and mental health. Biological processes have proven to be strikingly responsive to the psychosocial world.

The concept that nerves use chemicals to communicate with each other, first suggested early in this century, paved the way to an astonishingly rich body of knowledge that is expanding exponentially. The neurosciences have uncovered a wide variety of substances involved in regulating the brain and, thus, behavior. The field must reformulate its concepts about normal and pathological brain function constantly. For example, the discovery several years ago of a whole family of substances with opiate-like properties suggested entirely new hypotheses not only about the cause of addiction but also about depression and schizophrenia; it also

opened new avenues for the constant search for better drugs to treat major mental and addictive disorders. Dozens of neuroregulators probably remain to be discovered, each with a unique relevance to the brain, behavior, mental disorders, and addictions.

Better analytical methods for measuring substances in brain tissue and body fluids, including mass spectrometry, radioimmunoassay, and high performance liquid chromatography, foreshadow both diagnostic tests and the monitoring of drug concentrations to find the optimal therapeutic dose and to minimize side effects. New abilities to study brain processes in intact animals and in human beings are exciting. For example, investigators now can monitor electrical activity or obtain samples for chemical analyses from small brain regions as animals roam about freely or engage in specific tasks. For the first time, clinical researchers can conduct studies of the living human brain, using safe and minimally invasive techniques. Surface electrodes have been used in human studies for years, but sophisticated computer analyses recently have expanded the utility of the technique substantially. Both x-ray computed axial tomography (CAT) and nuclear magnetic resonance (NMR) imaging now provide detailed pictures of brain structures. Positron emission tomography (PET) is useful for monitoring some aspects of brain metabolism, and NMR spectroscopy may extend such capabilities greatly in the near future. These techniques provide powerful new probes with which to look for underlying abnormalities in individuals with severe mental or addictive disorders.

Major strides are being made toward elucidating physiological and neurochemical mechanisms involved in a number of important behaviors. For example, biological rhythms, including the sleep/wake cycle, are under active investigation. Compelling evidence indicates that these rhythms are altered in depression, and clinical researchers are testing whether restitution of such disturbed biorhythms is therapeutic for some people. Learning and memory under a variety of individual and group conditions also are being examined. Careful study even of such simple life forms as sea snails has been remarkably helpful in elucidating basic aspects of learning. Data from such research may clarify the origins and course of some types of dementia and learning problems.

Research in the psychological and social sciences is proceeding well on several fronts. Thus, researchers in neuropsychology have learned a great deal about regional specializations of the brain; such information is vital in work with stroke and seizure victims and also may be important for understanding symptoms in major mental disorders. Investigators using the tools of epidemiology have identified different forms of mental disorders and patterns of drug and alcohol use and abuse among varying subpopulations in this country and in other cultures. These data are needed to improve diagnostic reliability and validity and for developing more individually tailored treatment interventions. Other social scientists have found that social support mechanisms can alter a person's sensitivity to stressors to a remarkable degree, a discovery that may be useful in facilitating and sustaining recovery from mental and addictive disorders. Their findings fit nicely with the more general observation that psychological and social meaning can have a major role in determining the consequences to an individual of even the most stressful experiences; mechanisms through which such filters work are of great theoretical

and practical interest. Help-seeking behaviors are another important area of study that should be of use in developing more efficient health delivery systems. Rapid developments in mathematical and computer theory and the growing availability of powerful computers has greatly enhanced the feasibility of many forms of psychosocial research, while decreasing the cost.

The psychosocial disciplines already are contributing substantially to the clinical armamentarium. For example, cognitive and behavioral research is the basis for desensitization and exposure techniques, the best known therapy for patients with certain phobias. They also have led to innovative, increasingly effective programs for smoking prevention and cessation and for control of mild-to-moderate obesity. Well-done studies have shown consistently that psychosocial therapies also are effective for ambulatory nonpsychotic depression, mild-to-moderate anxiety, some forms of compulsion, sexual dysfunction and deviation, problems arising from acute crises and vocational or marital adjustments, and deficits in behavioral or social skills. Efforts are underway to find practical ways to mobilize social supports as a treatment intervention. More generally, mental health researchers have pioneered in developing objective clinical trials, perfecting such techniques as double-blind trials and cross-over designs and defining appropriate control groups.

Progress within one discipline in the biobehavioral sciences often is intertwined closely with advances in others. For example, the discovery of effective drug treatments for several major mental disorders was a strong stimulus for basic research on brain physiology, pharmacology, and biochemistry and for improved diagnostic and clinical procedures to assess drug effects. The fact that available drugs do not work for everyone and that they have unpleasant, sometimes dangerous side effects has fostered, in turn, a search for safer, more effective drugs and has encouraged consideration of psychological and social treatments that can be used alone or in combination with an appropriate drug. As a result, some depressed patients now can choose either drug or nondrug therapy, with equally good chances of success. Also, studies suggest that many schizophrenics can do well on lower doses of antipsychotic drugs and will function better longer, if people around them learn to reduce the emotional intensity of their interactions.

Recent attention to some specific populations has proven to be quite productive. For example, research on infants has revealed an unexpected early awareness of their surrounding environment and a remarkable array of social, emotional, and physical responses to it. This work has altered concepts of infancy profoundly, leading both to further research and to major shifts in social policy. For instance, investigators have begun to study ways of facilitating growth and development of premature infants, using physical stimulation such as stroking or rocking. Research suggests that requirements for effective stimulation are quite precise and that the right stimulus can enhance chances of survival markedly. At the level of public policy, agencies now try to arrange for adoptions within the first few weeks of life, if possible, to facilitate the early infant-caregiver relationship. Recent legislation to encourage continuity of foster care and early adoption also is based largely on findings that are emerging from this important area of research.

The research efforts within the ADAMHA mandate are and should continue to be directed toward goals far beyond treating specific mental disorders and addictions. Basic scientists are asking questions about such fundamental aspects of human existence as learning, sleep, aggression, and the details of psychological and social development. The potentials of this new knowledge are as awesome as were the discoveries in fields such as mathematics and astronomy. Lifestyle already contributes to many of the most pressing health problems in the United States, and the relative importance of behavioral factors almost certainly will continue to increase. Reversing this trend will require collaboration between the biobehavioral sciences and more traditional branches of medicine and public health.

Some General Funding Guidelines

Fulfilling the ADAMHA mandate demands strong support of basic research in all three of the major fields that contribute to an understanding of brain function and behavior--the psychological, social, and biological sciences. Fundamental discoveries in many different, seemingly unrelated settings often are crucial for producing clinical advances. As a result, support for broad areas of research frequently may yield a better outcome than does highly disease-targeted funding.

Strong programs in the basic neurosciences and psychosocial sciences are essential to ADAMHA's mission. The evolution of basic neuroscience into a discipline in its own right has largely resolved earlier controversies about who should support it: like biochemistry, neuroscience is a technique applicable to many different illnesses, and thus relevant to several institutes. Basic neuroscience is one key to understanding severe mental illnesses and addictions, but it also is relevant to neurological problems, to such cardiovascular diseases as hypertension, to some aging processes, and possibly to immunological responses and to cancer. Similarly, knowledge that must come from advances in the basic psychological and social sciences will be of great use to several NIH institutes, as already evidenced in the heart-disease prevention program of NHLBI. Even so, the unique questions that ADAMHA institutes ask about brain function and behavior argue for their continuing to be a major source of support for basic research in neuroscience and in psychosocial sciences.

The issue of overlapping research among institutes often is more a fear than a fact. For example, neuroscience research typically is allocated to some ADAMHA or NIH institute according to the disease state to which it seems most directly relevant. Naturally, information gained from one focus of the work may prove to be relevant to many other aspects of the field; but such an occurrence reflects mainly the often unpredictable flow of science. Experimental findings from seemingly divergent fields may converge suddenly to yield insights into some phenomenon of interest. The institutes typically apply the same basic scientific concepts and technology to different problems; so, given the small available pool, it is not surprising that researchers sometimes receive support for different aspects of their work from several institutes simultaneously. The Board believes that access to multiple funding sources should continue, when it appropriately utilizes a scientist's training and expertise. One of the quickest ways to foster quality research in understudied areas such as childhood mental disorders and alcoholism is to provide

incentives for talented researchers to consider how their current work might be relevant to this new problem.

In addition to supporting research along traditional disciplinary lines, ADAMHA should continue its efforts to identify and fund exemplary multidisciplinary projects. When done properly, such studies hold great promise of answering major questions about the underlying etiologies of mental disorders and addictive states. For example, examination of the interactions between biological processes and psychological and social factors--at both a basic science and a clinical level--may lead to a far more complete understanding of what addiction is and how it can best be treated. Attention also should be given to multidisciplinary approaches for studying large populations over time; with these admittedly expensive projects, ADAMHA should take steps to ensure the studies maximize their use of rare resources.

ADAMHA should increase its investment in research equipment and in facilities for investigators. Even in areas of great interest such as neuroscience, ADAMHA has done relatively little to help first-rate groups acquire the instrumentation needed to keep them abreast of the field. Researchers are turning to high technology to study mental disorders because it makes possible quantitative measures of important parameters of brain function--most of which have become available only within the past decade. Some technologies have high startup costs, for example, positron emission tomography (PET) and nuclear magnetic resonance (NMR) imaging and spectroscopy; yet the neurosciences must develop capabilities in these areas to facilitate their applications to studies of the brain. Strong support from ADAMHA can help ensure that these powerful new techniques are applied expeditiously to questions about mental and addictive disorders.

Equipment and facilities are the vital infrastructure for research. Biological and psychosocial research groups throughout the country have pressing needs in these areas that go beyond the desire to acquire and apply the latest technological innovations. Many neuroscientists now must conduct their research with outmoded equipment that lacks the sensitivity and accuracy demanded of contemporary work in fields such as biochemistry, analytic chemistry, and neurophysiology. Some psychosocial researchers also have urgent infrastructure needs, for example, large computers and controlled environment settings for individual and group studies. Traditionally, with the overall extreme shortage of funds, only a tiny fraction of the ADAMHA budget has gone to support equipment and facilities; yet, for many outstanding programs, replacement and upgrading of equipment has become imperative. Such investments must be considered carefully; but, in many instances, continued progress will be impossible without active assistance from ADAMHA.

Good, generalizable clinical research on mental and addictive disorders has developed slowly. It required identification of and innovative solutions for a variety of problems unique to such populations. Valid clinical research needs long-term, well-organized facilities with ready access to appropriate subject populations, reliable rating scales for relevant behaviors and psychological states, resources for analyzing large amounts of complex data, and close attention to maintaining good care of study volunteers. ADAMHA was instrumental in facilitating the development of such centers and should make every effort to ensure their continued stability

and to increase funding as needed for outstanding centers to maintain optimal levels of clinical care and research.

Research Funding Mechanisms

ADAMHA has employed diverse funding mechanisms successfully, among them being small grants, new investigator awards, individual research grants, program project grants, research scientist awards, clinical research centers, and cooperative agreements for collaborative studies. It should continue its use of multiple support mechanisms, in recognition of the many ways in which excellent research can be organized. Peer review of investigator-initiated proposals remains the most acceptable and effective way known to assign priorities for funding.

Most ADAMHA grants support research that will take several years to complete. Those funded for more than one year are reviewed annually for scientific merit, but the investigator does not compete with new grants until the end of the grant cycle. One effect of the reduction in research funds has been a decrease in the funding period; grants for over three years now are rare. For many research projects, three years or less have proven to be reasonable and appropriate; however, longer cycles would be beneficial in some cases. The importance of stable funding for longitudinal studies was mentioned already; having only two to four grant cycles during a ten to twenty year project would foster such stability. Most prospective studies, for example, those involving risk-factor analysis or randomized treatment outcome, need at least two to three years of support for implementation, data gathering, and data analysis. Longer cycles, possibly five years, also might be appropriate for outstanding investigators or for programs with demonstrated and sustained productivity. In such instances, a yearly review of the progress and scientific merit of the work should be adequate to ensure continued quality and certainly would be less disruptive than a full-scale grant renewal. An ADAMHA taskforce could establish guidelines for such selected cases.

Easier mechanisms are needed to fund cross-disciplinary projects, both within ADAMHA and between ADAMHA and NIH or other parts of the Public Health Service. For example, Alzheimer's disease is within the mandate of NIMH, NIA, and NINCDS. ADAMHA researchers have made valuable contributions to the study of the psychosocial and basic neurobiological aspects of the dementias. Presently, to seek additional funding from either of the NIH institutes, they must submit a new grant that differs from the work being done under NIMH auspices, needlessly splintering their work into "fundable" units. Behavioral aspects of physical diseases are another striking example in which basic research supported by ADAMHA is of clear relevance to concerns of the NIH institutes. Collaborative ventures among the institutes to fund mutually relevant studies would be enormously beneficial to the research community.

Manpower Training Needs

A cadre of able investigators already are studying many aspects of mental and addictive disorders, but rapid evolution in the biobehavioral sciences constantly creates demands for new types of specially trained researchers, often without diminishing the continued needs of existing specialties. Current research areas of identified special need include those related to childhood mental disorders and to alcoholism.

ADAMHA has a history of supporting a small number of first-rate graduate studies toward a Ph.D. both through individual grants and with program training grants. Such funding is crucial for several disciplines within the biobehavioral sciences and should continue at pre- and postdoctoral levels. Regular reassessments can help to ensure that the overall level of funding is adequate and provide chances to alter funding patterns to reflect changes in research opportunities. In this field, a clinical perspective often is an asset even with the most basic research. For that reason, ADAMHA should develop some programs through which biobehavioral scientists without clinical training have a chance to see first hand the actual clinical presentation of the disorders they are studying.

Current ADAMHA funding mechanisms do not meet the needs of physicians who want research training, despite a serious lack of medical researchers to study mental and addictive disorders. For many years, the NIH has funded Medical Scientists Training Programs (MSTP) in top medical schools across the country; the programs provide stipends and tuition for trainees working toward both an M.D. and a Ph.D., usually in exchange for a service commitment once training is over. This has been a highly effective way to train physician researchers; a strikingly large percentage of these gifted young people have stayed in academic careers after fulfilling the service commitment. ADAMHA should explore the relative merits of creating its own MSTP or joining NIH in a venture that would add positions to existing programs for people with research interests relevant to the ADAMHA mandate. In addition, more and better research opportunities are needed for physicians during residency. Across the country, few residents who have interests in research careers in the mental health field can reasonably accept available postdoctoral positions, which are designed for recent Ph.D. graduates. Both low stipends and programmatic restrictions of such positions are incompatible with the realities of most residency training programs. Salary stipends should at least match those for medical postdoctoral trainees in the ADAMHA and NIH intramural programs, and special consideration should be given to the needs of those doing research while they continue their medical education.

Two excellent ADAMHA programs should be continued and strengthened. Research Scientist Development Awards and senior-level Research Scientist Awards enable particularly able persons to devote their energies to research and research training, without having to draw salary support from project-specific grants. These funding mechanisms are an excellent way to encourage the best scientists to continue their academic pursuits. But, ADAMHA now needs funds for additional positions, to accommodate the growing number of deserving applicants; also, stipends should be increased to a level that is commensurate with existing academic salaries.

The Need for Increased Federal Funding

For many areas of research within ADAMHA's mandate, available funding is too low to take advantage of exciting research opportunities--or even to foster rational development of the field. Research related to childhood mental disorders and basic research related to alcoholism exemplify this problem. Each of the three ADAMHA institutes is responsible for research on pressing health problems that merit additional support. Even for some of the most difficult of these problems, the existence of promising approaches to their solution argue for increased research support. The Federal government is the only possible source for the needed funds. In 1983, the last year for which actual expenditures are available, the ADAMHA institutes spent \$238 million overall for direct research costs; \$273 million was budgeted for 1984.

Mental illnesses and addictions do not enjoy the history of private philanthropy that exists for some other types of severe illness, and there is no evidence that this is likely to change. When the Board reviewed support areas for the 2,800 largest foundations in the United States, it found only 970 that make donations on a national or regional basis. Of those, one listed alcohol as its major focus and another listed drug abuse as a major focus. Fewer than 30 mentioned mental health, psychiatry, or psychology as even a minor interest. The recent entry of the MacArthur Foundation into the mental health field is a heartening but notable exception to this pattern.

Individual donors also provide little support for research on mental disorders and addictive states. In other areas of biomedical research, private donations provide flexible funds for developing facilities, aiding talented students, facilitating rapid testing of new ideas, underwriting development of new types of equipment or measurement techniques, providing matching funds, and supporting faculty salaries for able investigators. Yet, despite the widespread prevalence of mental disorders and addictions, only a few farsighted people support these areas. The general scarcity of funds underscores the importance of the federal role in research within the ADAMHA domain.

The preceding material leads one ineluctably to the conclusion that federal support for research on mental disorders and addictive states should--indeed must--expand markedly. The disorders already account for a large and steadily increasing portion of the total burden of illness in the United States, whether the index used is mortality, morbidity, human suffering, or economic cost. Great advances have been made in acquiring the research tools and conceptual frameworks needed as a foundation for finding solutions to these problems. Undoubtedly, several areas within the biobehavioral sciences, especially those at the interface of traditional disciplines, would benefit from attracting additional talented, well-trained scientists. Still, the pool of available researchers has swelled over the past decade, both with newly trained young people and with experienced investigators from other fields whose interests drew them into the biobehavioral area. Taken together, these developments argue persuasively for the appropriateness and potential benefits of vigorous and sustained support for basic research on understanding behavior and brain function and applied research for improving the prevention, diagnosis, and treatment of mental and addictive disorders.

In the past few years, a number of thoughtful reports have documented the urgent needs, overwhelming costs, and great research promise of various areas within the ADAMHA mandate (Appendix A). Some of them clearly have had beneficial effects, drawing attention to problems where needs were especially critical and sometimes at least temporarily stemming the steady decrease in buying power that has characterized ADAMHA budgets for over 15 years. Like earlier efforts, this report identifies some areas of research, for example, mental disorders of childhood and adolescence and alcoholism, where needs for increased support are conspicuous even in the context of the field's overall straits. However, for years, ADAMHA has had less and less ability to sponsor the range of studies needed to address increasingly pressing problems and rich research opportunities. As a result, it now faces such severe dilemmas that patchwork attention to particular programs no longer is tenable. Rather, the overall research base that ADAMHA can support must expand substantially, so that planners once again can begin to allocate support rationally among specific areas within the field.

Reasonably objective standards exist for assessing the relative contribution mental and addictive disorders make to the overall burden of illness in the United States and even judging the scientific readiness of relevant research fields. However, no known formula can convert such information into an appropriate research budget; this latter exercise must rely more on experience and analogy. Previous reports about aspects of research on mental and addictive disorders typically have stopped short of this practical yet critical consideration, so the Board concluded that it should offer suggestions about the level of support needed.

As a starting point, the Board examined the funding history of NIMH, which had its inflation-adjusted peak research budget in 1966. As discussed earlier, the Biomedical Research and Development Price Index, which reflects the effects of inflation on major sources of cost in research, rose from 44.2 in 1966 to 135.2 in 1983. In 1966, the total NIMH research budget was \$100 million, so an inflation-indexed NIMH research budget for 1983 should have been \$307 million--compared with actual 1983 allocations of \$158 million for direct research costs. Using a completely different yardstick, had NIMH just kept pace over the past 12 years with increases in the NIH research budget, its research budget would have grown to \$312 million by 1984. Neither of these calculations includes increases in research allocations that could be justified on the basis of existing research opportunities and available research personnel. Not surprisingly, Board members held widely differing views about the appropriate size of such additional increases; as a result, overall suggested research budgets for NIMH ranged from a minimum of \$300 million to figures several times that amount.

For NIAAA, the board consulted the IOM study Alcoholism and Related Problems: Opportunities for Research, published in 1980, which suggested that "increasing current research budgets by 50 percent in each of the next three years might begin to make the desired impact" of fostering a vigorous research effort on the problems of alcoholism and alcohol abuse (p. 23). That study and other efforts have had a salutary effect: the NIAAA spent \$22 million on research in 1979 and \$33 million in 1983--an increase of 50 percent; but, based on the IOM recommendation, and adding a correction for inflation, the 1983 NIAAA research budget should have

been \$102 million. As noted earlier, the Board concurred with the overall findings and recommendations of the 1980 study, and Board members agreed that \$100 million was a reasonable, lower estimate of needed support for research on alcohol problems.

The Board is unaware of any comparable study of the NIDA research program. However, current research expenditures per afflicted individual resemble those for major mental disorders in the NIMH domain. Also, NIDA has sponsored some especially exciting research over the past decade that led directly to the discovery of endogenous opioid peptides and engendered important reformulations of hypotheses about brain function. Furthermore, NIDA is seeking to adopt an increasingly broad view of its mandate, to include both classical addictive processes and strong compulsions or habits such as cigarette smoking. Given these considerations, the Board members agreed that at least a doubling of the NIDA research budget, which was \$47 million in 1983, was appropriate.

The recommended increases are so substantial that questions can and should be raised about how best to institute them. In many instances, existing research programs could make use of an expansion of support immediately. In others, preparatory work is needed in the form of training programs, with a slower increase in research support as personnel become available. A detailed examination of the entire ADAMHA research portfolio lies far beyond the scope of this report. The Board recommends that the ADAMHA Administrator authorize and oversee the development of a plan for expansion, calling on the constituent agencies and on outside groups for advice in setting immediate and long-range goals and priorities for each Institute. That plan should provide detailed recommendations on how best to utilize, in a five-year timespan, the following annual ADAMHA allocations for research and research training, in constant 1983 dollars:

National Institute on Alcoholism and Alcohol Abuse	\$100 million
National Institute on Drug Abuse	\$100 million
National Institute of Mental Health	\$300 million

The Board is sensitive to the problems inherent in a call for more funding for any cause; yet, the data are too compelling to do otherwise. Board members agreed on the above figures as minimal targets, in an effort to temper the legitimate needs of those affected by mental disorders and addictions with a recognition of this nation's current fiscal constraints. Many researchers from a wide range of backgrounds argued cogently that, given current and anticipated costs to society and excellent prospects for progress in the field, levels of support should be much higher. Several suggested that a more fitting target for the total annual ADAMHA research budget would be \$750 million to \$1 billion.

The United States must make a strong commitment to reducing the enormous burden of mental disorders and addictive states. Over the past two decades, a large decline in the real buying power of research allocations for the ADAMHA institutes has hampered efforts to carry out their mandate, and no administrative streamlining or acceptable programmatic changes will relieve the strain. Numerous research leads are rising out of the impressive scientific progress already made, and they merit vigorous support. Given the magnitude of the problem, even partial reduction

of the costs to society of such major disorders as schizophrenia and severe childhood mental disorders would quickly recover the recommended increases in research budgets. Clear acknowledgment now of the importance of these disorders, expressed positively in the form of more fitting levels of support for research, could yield immense dividends in the decades to come.

Appendix A

Relevant Institute of Medicine Publications

Listed below are major works of the Institute of Medicine within the past seven years that are directly relevant to the disorders and research considered in this report and that the Board used in its deliberations.

The Current Burden of Illness in the United States. An occasional paper of the Institute of Medicine by D.P. Rice, J.J. Feldman, and K.L. White. Ann Arbor: University Microfilms International, 1977. UMI Order No. 2008427.

Adolescent Behavior and Health. Summary of a Conference by Division of Health Sciences Policy, Division of Health Promotion and Disease Prevention. Springfield, VA: National Technical Information Service, 1978. NTIS Accession No. PB-294-362/AS.

Sleeping Pills, Insomnia, and Medical Practice. Report of a Study by a Committee of the Institute of Medicine, National Academy of Sciences. Washington, D.C.: National Academy Press, 1979.

Healthy People, The Surgeon General's Report on Health Promotion and Disease Prevention, Vol. II - Background Papers. Washington, D.C.: U.S. Government Printing Office, 1979. GPO Stock No. 017-001-00417-1.

Mental Health Services in General Health Care. Summary of the Invitational Conference on the Provision of Mental Health Services in Primary Care Settings, April, 1979. Springfield, VA: National Technical Information Service (NTIS Accession No. PB-125420), 1979. Also published as Mental Health Services in Primary Care Settings: Report of a Conference. D. Parron, Ed. Washington, D.C.: Government Printing Office, 1980. DHHS Publication No. (ADM) 80-995.

Alcoholism, Alcohol Abuse and Related Problems: Opportunities for Research. Report of a Study by a Committee of the Institute of Medicine, National Academy of Sciences. Washington, D.C.: National Academy Press, 1980.

Stress and Human Health. Report of a Study by a Committee of the Institute of Medicine, National Academy of Sciences. G.R. Elliott and C. Eisdorfer, Eds. New York: Springer Publishing Co., 1981.

Smoking and Behavior. Summary of an Institute of Medicine Invitational Conference, held September 1979. Springfield, VA: National Technical Information Service, 1980. NTIS Accession No. PB-80-201585. This constitutes Interim Report No. 1 of the study Health and Behavior: A Research Agenda.

- Combining Psychosocial and Drug Therapy: Hypertension, Depression, and Diabetes. Summary of an Institute of Medicine Invitational Conference, held May 1980. D.L. Parron and F. Solomon, Eds. Washington, D.C.: National Academy Press, 1981. This constitutes Interim Report No. 2 of the study Health and Behavior: A Research Agenda.
- Biobehavioral Factors in Sudden Cardiac Death. Summary of an Institute of Medicine Invitational Conference, held August 1980. F. Solomon, D.L. Parron, and P.B. Dews, Eds. Washington, D.C.: National Academy Press, 1981. This constitutes Interim Report No. 3 of the study Health and Behavior: A Research Agenda.
- Infants at Risk for Developmental Dysfunction. Summary of an Institute of Medicine Invitational Conference, held August 1980. D.L. Parron, and L. Eisenberg, Eds. Washington, D.C.: National Academy Press, 1982. This constitutes Interim Report No. 4 of the study Health and Behavior: A Research Agenda.
- Health, Behavior and Aging. Summary of an Institute of Medicine Invitational Conference, held January 1981. D.L. Parron, F. Solomon, and J. Rodin, Eds. Washington, D.C.: National Academy Press, 1981. This constitutes Interim Report No. 5 of the study Health and Behavior: A Research Agenda.
- Behavior, Health Risks, and Social Disadvantage. Summary of an Institute of Medicine Invitational Conference, held May 1981. D.L. Parron, F. Solomon, and C.D. Jenkins, Eds. Washington, D.C.: National Academy Press, 1982. This constitutes Interim Report No. 6 of the study Health and Behavior: A Research Agenda.
- Health and Behavior: Frontiers of Research in the Biobehavioral Sciences. Report of a Study by a Committee of the Institute of Medicine, National Academy of Sciences. D.A. Hamburg, G.R. Elliott, and D.L. Parron, Eds. Washington, D.C.: National Academy Press, 1982. This constitutes the final report of the study Health and Behavior: A Research Agenda.
- Marijuana and Health. Report of a Study by a Committee of the Institute of Medicine, National Academy of Sciences. Washington, D.C.: National Academy Press, 1982.
- Report of the Research Briefing Panel on Neuroscience, in Research Briefings, 1982, pp. 81-98. Committee on Science, Engineering, and Public Policy. Washington, D.C.: National Academy Press, 1983.
- Bereavement: Reactions, Consequences, and Care. Report of a Study by a Committee of the Institute of Medicine, National Academy of Sciences. M. Osterweis, F. Solomon, and M. Green, Eds. Washington, D.C.: National Academy Press, 1984.

Appendix B

Unpublished Background Papers Prepared for the Board

Contributors prepared these reviews of special topics at the request of the Board on Mental Health and Behavioral Medicine of the Institute of Medicine, National Academy of Sciences, for its use in preparing this report. Although these papers are not available for distribution, the Board wishes to acknowledge the valuable contribution each of these individuals made to its deliberations.

The Scope of Mental Health Problems

Beatrix Hamburg

Affective Disorders

Jack D. Barchas, Philip A. Berger,
Patricia R. Barchas, and Glen R. Elliott

Schizophrenia and the Psychoses

Philip A. Berger, Jack D. Barchas,
Patricia R. Barchas, and Glen R. Elliott

The Abuse of Psychoactive Substances

Philip A. Berger and Meredith D. Berger

Alcohol Abuse

Glen R. Elliott and Philip A. Berger

Childhood Disorders

Albert J. Solnit, Donald Cohen,
Thomas Anders, and Roland D. Ciaranello

Disorders of Aging

Lissy F. Jarvik

Basic Research Issues in Behavioral Medicine

Neal E. Miller

