NIMH Research Domain Criteria (RDoC)

Draft 3.1: June, 2011

Over the past several decades, an increasingly comprehensive body of research in genetics, neuroscience, and behavioral science has transformed our understanding of how the brain produces adaptive behavior, and the ways in which normal functioning becomes disrupted in various forms of mental disorders. In order to speed the translation of this new knowledge to clinical issues, the NIMH included in its new strategic plan Strategy 1.4: “Develop, for research purposes, new ways of classifying mental disorders based on dimensions of observable behavior and neurobiological measures.” (For the full text, see **http://www.nimh.nih.gov/about/strategic-planning-reports/index.shtml#strategic-objective1**). The implementation of this strategy has been named the Research Domain Criteria Project (RDoC). The purpose of this document is to describe the RDoC project in order to acquaint the field with its nature and direction, and to facilitate commentary from scientists and other interested stakeholders regarding both general and specific aspects of the RDoC approach.

Background

Across all areas of medicine, research in genomics, cell biology, and pathophysiology is revolutionizing diagnosis and treatment. In disorders as diverse as cancer, heart disease, diabetes, and inflammatory bowel disease, the discovery of identifiable subtypes within broad clinical phenotypes has led to more specific, more effective treatments or identification of new targets for prevention. Research in mental disorders is also developing quickly: Novel data about genomic factors and the role of particular brain circuits are reported almost monthly. However, new findings on mental disorders have had limited clinical impact, partly because they map only moderately onto current diagnostic categories for mental illness. Thus, some of the risk genes for psychotic disorders appear to be associated with both schizophrenia and bipolar disorder and the same prefrontal region has been implicated in depression and PTSD. In contrast to cancer and heart disease, where research has identified subtypes of common disease, it appears that the biological findings with mental disorders are relatively non-specific; could specificity in fact exist, but not for the currently recognized clinical categories? This question leads to a consideration of how current categories were derived.

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Currently, diagnosis in mental disorders is based on clinical observation and patients' phenomenological symptom reports. This system, implemented with the innovative Diagnostic and Statistical Manual-III (DSM-III) in 1980 and refined in the current DSM-IV-TR (Text Revision), has served well to improve diagnostic reliability in both clinical practice and research. The diagnostic categories represented in the DSM-IV and the International Classification of Diseases-10 (ICD-10, containing virtually identical disorder codes) remain the contemporary consensus standard for how mental disorders are diagnosed and treated, and are formally implemented in insurance billing, FDA requirements for drug trials, and many other institutional usages. By default, current diagnoses have also become the predominant standard for reviewing and awarding research grants.

However, in antedating contemporary neuroscience research, the current diagnostic system is not informed by recent breakthroughs in genetics; and molecular, cellular and systems neuroscience. Indeed, it would have been surprising if the clusters of complex behaviors identified clinically were to map on a one-to-one basis onto specific genes or neurobiological systems. As it turns out, most genetic findings and neural circuit maps appear either to link to many different currently recognized syndromes or to distinct subgroups within syndromes. If we assume that the clinical syndromes based on subjective symptoms are unique and unitary disorders, we undercut the power of biology to identify illnesses linked to pathophysiology and we limit the development of more specific treatments. Imagine treating all chest pain as a single syndrome without the advantage of EKG, imaging, and plasma enzymes. In the diagnosis of mental disorders when all we had were subjective complaints (cf. chest pain), a diagnostic system limited to clinical presentation could confer reliability and consistency but not validity. To date, there has been general consensus that the science is not yet well enough developed to permit neuroscience-based classification. However, at some point, it is necessary to instantiate such approaches if the field is ever to reach the point where advances in genomics, pathophysiology, and behavioral science can inform diagnosis in a meaningful way. RDoC represents the beginning of such a long-term project.

RDoC is intended as a framework to guide classification of patients for research studies, not as an immediately useful clinical tool. While the hope is that a new way forward for clinical diagnosis will emerge sooner rather than later, the initial steps must be to build a sufficient research foundation that can eventually inform the best approaches for clinical diagnosis and treatment. It is hoped that by creating a framework that interfaces directly with genomics, neuroscience, and behavioral science, progress in explicating etiology and suggesting new treatments will be markedly facilitated.

Method

RDoC will follow three guiding principles, all diverging from current diagnostic approaches.

First, RDoC is conceived as a dimensional system (reflecting, e.g., circuit-level measurements, behavioral activity, etc.) spanning the range from normal to abnormal. As with dimensions like hypertension or cholesterolemia in other areas of medicine, this approach incurs both the problem and advantage of defining cutpoints for the definition and extent of pathology – e.g., mild, moderate, and severe. (To the extent that DSM-V introduces dimensions in addition to classes, the crosswalks to RDoC dimensions may be enhanced.)

Second, RDoC is agnostic about current disorder categories. The intent is to generate classifications stemming from basic behavioral neuroscience. Rather than starting with an illness definition and seeking its neurobiological underpinnings, RDoC begins with current understandings of behavior-brain relationships and links them to clinical phenomena.

Third, RDoC will use several different units of analysis in defining constructs for study (e.g., imaging, physiological activity, behavior, and self-reports of symptoms). Indeed, RDoC, as a research framework, has been developed with the explicit goal of permitting investigators to choose an independent variable from one of several different units of analysis. The details of this approach are explained next.

The RDoC research framework can be considered as a matrix whose **rows** correspond to specified dimensions of function; these are explicitly termed "Constructs," i.e., a concept summarizing data about a specified functional dimension of behavior (and implementing genes and circuits) that is subject to

continual refinement with advances in science. Constructs represent the fundamental unit of analysis in this system, and it is anticipated that most studies would focus on one construct (or perhaps compare two constructs on relevant measures). Related constructs are grouped into major Domains of functioning, reflecting contemporary thinking about major aspects of motivation, cognition, and social behavior; the five domains are Negative Valence Systems (i.e., systems for aversive motivation), Positive Valence Systems, Cognitive Systems, Systems for Social Processes, and Arousal/Regulatory Systems. The **columns** of the matrix represent different classes of variables (or units of analysis) used to study the domains/constructs. Seven such classes have been specified; these are genes, molecules, cells, neural circuits, physiology (e.g. cortisol, heart rate, startle reflex), behaviors, and self-reports. Circuits represent the core aspect of these classes of variables – both because they are central to the various biological and behavioral levels of analysis, and because they are used to constrain the number of constructs that are defined. Investigators can select any level of analysis to be the independent variable for classification (or multiple levels in some cases, e.g., behavioral functioning stratified by a genetic polymorphism), and dependent variables can be selected from multiple columns. In addition, since constructs are typically studied in the context of particular scientific paradigms, a column for "paradigms" has been added; obviously, however, paradigms do not represent units of analysis.

Three criteria guided the selection of the draft list of candidate constructs presented here. First, the inclusion of a construct was constrained by whether a particular brain circuit or area could reasonably be specified that implements that dimension of behavior. Given the complexity of the brain and of behavior, this was more ambiguous in some cases than others; some constructs, such as attention, reflect activity spread relatively diffusely over many brain areas, while attachment behavior may similarly reflect neurotransmitter and hormonal functions (e.g., oxytocin) acting at disparate locations throughout the brain. Second, an attempt was made to maintain a reasonable "grain size" that would permit a tractable listing of the major functional dimensions of behavior. While it is recognized that there may be important and meaningful sub-constructs that could be considered (e.g., various types of aggression), an overly specified list could result in an unwieldy and excessively long listing. Third, the constructs are based on current literatures that have provided a neurobehavioral research base for each of the entries.

The draft RDoC matrix is listed in the table below, followed by examples of how the classification system might be used and several points of clarification. Dimensional constructs are listed in the rows. Below the matrix, several constructs are listed to provide examples of brain circuits and/or neurotransmitters that help define and constrain each one, along with a brief indication, where appropriate, of constructs representing the dimension's opposite pole; note that listings of circuit components and neurotransmitters are meant to be illustrative, not exhaustive. Constructs are grouped into five major domain areas as listed above. **It is important to emphasize that these particular domains and constructs are simply starting points that are not definitive or set in concrete**. We expect these to change dynamically with input from the field, and as future research is conducted. The keys here are the overall framework that we are suggesting, and the process for its development.

Research Domain Criteria Matrix

Domain **Construct** ***Subconstruct***	**——— Units of Analysis ———**							
	Genes	**Molecules**	**Cells**	**Circuits**	**Physiology**	**Behavior**	**Self-Reports**	**Paradigms**
Negative Valence Systems								
Acute threat ("fear")								
Potential threat ("anxiety")								

Domain Construct *Subconstruct*	Units of Analysis							
	Genes	Molecules	Cells	Circuits	Physiology	Behavior	Self-Reports	Paradigms
Sustained threat								
Loss								
Frustrative nonreward								
Positive Valence Systems								
Approach motivation								
Reward valuation								
Effort valuation / Willingness to work								
Expectancy / Reward prediction error								
Action selection / Preference-based decision making								
Initial responsiveness to reward								
Sustained responsiveness to reward								
Reward learning								
Habit								
Cognitive Systems								
Attention								
Perception								
Visual Perception								
Auditory Perception								
Olfactory Somatosensory								

Domain Construct *Subconstruct*	Units of Analysis Genes	Molecules	Cells	Circuits	Physiology	Behavior	Self-Reports	Paradigms
Multimodal Perception								
Declarative memory								
Language behavior								
Cognitive (effortful) control								
Goal Selection								
Updating								
Representation and Maintenance								
Response Selection, Inhibition or Suppression								
Performance Monitoring								
Working memory ***** The Working Memory Workshop created a Matrix with a different format. Please see the Working Memory Workshop Proceedings document to view the Matrix for Working Memory and its subconstructs. *****								
Active Maintenance								
Flexible Updating								
Limited Capacity								
Interference Control								
Systems for Social Processes								
Affiliation and attachment								
Attachment formation and maintenance								

Domain Construct *Subconstruct*	Units of Analysis							
	Genes	Molecules	Cells	Circuits	Physiology	Behavior	Self-Reports	Paradigms
Social Communication								
Reception of Facial Communication								
Production of Facial Communication								
Reception of Non-Facial Communication								
Production of Non-Facial Communication								
Perception and Understanding of Self								
Agency								
Self-Knowledge								
Perception and Understanding of Others								
Animacy Perception								
Action Perception								
Understanding Mental States								
Arousal and Regulatory Systems								
Arousal								
Circadian Rhythms								
Sleep and wakefulness								

Notes regarding the Units of Analysis

"Circuits" can refer to measurements of particular circuits as studied by neuroimaging techniques, and/or other measures validated by animal models or functional neuroimaging (e.g., emotion-modulated startle, event-related potentials).

"Physiology" refers to measures that are well-established indices of certain constructs, but that do

necessarily not tap circuits directly (e.g., heart rate, event-related potentials).
"Behavior" can refer variously to behavioral tasks (e.g., a working memory task), or to behavioral observations.
"Self-reports" refer to interview scales, questionnaires, or other instruments that may encompass normal-range and/or abnormal aspects of the dimension of interest.

Examples of Constructs (individual entries) within Domains (boldface)

Negative Valence Systems

Fear (opposite pole, – fearlessness): amygdala, hippocampus, interactions with ventromedial PFC
Potential threat: HPA axis, BNST, hippocampus; CRF, cortisol

Positive Valence Systems

Approach motivation (opposite pole – anhedonia): mesolimbic dopamine pathway
Habit-based behavior (including OCD spectrum): orbitofrontal cortex, thalamus, dorsal striatum

Cognitive Systems

Working memory: dorsolateral PFC, other areas in PFC
Cognitive (Effortful) control (opposite pole – impulsivity, disinhibition, externalizing): anterior cingulate gyrus, various areas of medial and lateral PFC

Systems for Social Processes

Social dominance: distributed cortical activity, mesolimbic dopamine systems; testosterone, serotonin
Facial expression recognition: ventral visual stream, fusiform gyrus
Self-representational circuits: dorsal & posterior ACC, insula

Arousal/Regulatory Processes

Stress regulation: raphe nuclei circuits; serotonin
Facilitated stimulus processing: locus coeruleus circuit; norepinephrine
Readiness for stimulus processing and responding: brain resting state network

Abbreviations:

PFC: Pre-frontal cortex
HPA: hypothalamic-pituitary axis
BNST: bed nucleus of the stria terminalis
CRF: corticotrophin releasing factor
OCD: obsessive-compulsive disorder
ACC: anterior cingulate cortex

Given that RDoC is a classification framework, how might the scheme work in actual practice, given the goals of (1) permitting widely differing independent variables and (2) implementing a dimensional system that allows variance extending down into what would be regarded as sub-threshold psychopathology? Two general approaches are as follows. The first is to include all patients presenting for treatment at a given type of treatment facility, as in the second example below; the statistical approach then becomes one of regression. The second approach is to specify a particular criterion for selecting multiple groups – e.g., patients who score more than one standard deviation below the mean on a cognitive task, patients who show significant activation in a specified brain area on a neuroimaging task – and compare these to other patients not meeting the criterion and/or to a non-clinical control

group. In any case, exclusions for co-morbid conditions would be expected to be much less stringent (although the usual exclusions such as other medical or neurological disorders, extreme substance abuse, etc. could still apply). Manuscripts submitted under RDoC will be expected to state how many patients were screened for inclusion in the study, and the reasons for exclusion.

Example Studies

Two example studies are listed in order to illustrate the types of studies that might be conducted within the RDoC framework. For clarity, the variables used to classify subjects are reiterated at the end of each example.

1. Recent studies have shown that a number of genes reported to confer risk for schizophrenia, such as DISC1 (“Disrupted in schizophrenia”) and neuregulin, actually appear to be similar in risk for unipolar and bipolar mood disorders. These findings are consistent with a number of recent papers questioning the classical Kraepelinian distinction between schizophrenia and bipolar disorder; however, little data are available to evaluate psychotic disorders as a spectrum since studies almost always focus on one or the other, and patients falling short of DSM/ICD criteria are excluded. Thus, in one potential design, inclusion criteria might simply consist of all patients seen for evaluation at a psychotic disorders treatment unit. The independent variable might comprise two groups of patients: One group would be positive and the other negative for one or more risk gene configurations (SNP or CNV), with the groups matched on demographics such as age, sex, and education. Dependent variables could be responses to a set of cognitive paradigms, and clinical status on a variety of symptom measures. Analyses would be conducted to compare the pattern of differences in responses to the cognitive or emotional tasks in patients who are positive and negative for the risk configurations. The results of studies of this type could contribute to knowledge about the particular types and severity of behavioral and/or neurobiological deficits that tend to be associated with a given risk gene; in turn, such results could help build a foundation to study mechanisms by which a particular candidate gene contributes to adverse effects. Eventually such research might lead to redefining how psychotic disorders are conceptualized. Classification variables: In this example, the domain under study is Cognition (possibly comparing two to three constructs such as working memory versus declarative memory). The independent variable for classification is the risk gene configuration(s), and the dependent variables comprise performance on the various cognitive tasks. (It is possible that DSM diagnosis, or some other set of psychiatric symptoms, might serve as a second independent, between-subjects variable; however, an emphasis on studying mechanisms would dictate that the sample not be constrained to patients with only schizophrenia or bipolar disorder – i.e., inclusion criteria should incorporate those with schizoaffective disorder, delusional disorder, psychotic disorder NOS, etc.)
2. A large number of studies have examined neuroimaging responses to various types of emotional challenges in patients with a particular mood or anxiety disorder, compared to non-clinical controls. Frequently, the conclusion is that disorder X is characterized by an abnormality in task Y – such as emotion regulation, activation of a particular circuit or brain area (e.g., amygdala, ventromedial PFC), or response to some emotion-related task. However, such abnormal mechanisms appear to be involved in many different disorders, while on the other hand, not all patients with a given diagnosis necessarily show the abnormality – suggesting that there are fundamental mechanisms in common across these disorders. A design to study fear circuitry might thus have as inclusion criteria all patients presenting at an anxiety disorders clinic. Classification variables: The construct of interest is Fear/extinction, in the domain of Negative Affect. The independent variable for grouping would be the extent of responding to fearful stimuli using a measure such as amygdala response (from fMRI) or fear-potentiated startle (i.e., a circuit-level variable). Dependent variables would be symptom measures on various fear and distress measures, in order to test hypotheses about mechanisms by which hyper-reactivity and hypo-reactivity to threat cues affect the nature and severity of presenting symptoms. As an outcome of such research, these results might generate predictive validity studies leading to improved treatment selection or new pharmacological targets for intervention.

Developmental and Environmental Aspects

The RDoC concept is organized around basic neural circuits, their genetic and molecular/cellular building blocks, and the dimensions of functioning that they implement. There are two highly important areas of mental disorders research that are thus not represented in the matrix per se, but are considered to be critical elements in research fostered by RDoC. These two areas are developmental aspects and interactions with the environment. The intent is that the RDoC matrix will enhance the study of both areas by promoting a systematic focus on their relationship to specific circuits and functions.

Developmental aspects. Mental disorders are increasingly viewed as neurodevelopmental disorders in one way or another. Therefore, addressing development issues across various phases of the life span represents a critical consideration that is implicit to the RDoC framework, and might be considered as a third dimension in the matrix. The types of constructs typically found in the child temperament literature are (not coincidentally) similar to the RDoC domains, and many areas of the child psychopathology literature (e.g., broadly addressed to Internalizing or Externalizing problems) serve as a more compatible model for a dimensionally-based approach compared to the highly specified categories of adult psychopathology. Four brief examples might be given of life-span goals that could be addressed within the RDoC framework: (1) Further explicate the longitudinal course of adolescent brain maturation and synaptic pruning to identify genes and circuit development factors associated with departures from normal developmental functioning, and points in prodromal stages where intervention might particularly be targeted; (2) Evaluate the extent to which the recruitment of additional cortical areas during task performance or emotional challenge in elderly subjects predicts resilience against onset or deterioration of course in mental disorders; (3) Generate improved explication of the construct of cognitive control (or effortful control), relative to disentangling current controversies regarding ADHD, juvenile bipolar disorder, conduct disorder, etc.; (4) Specify the mechanisms regarding developmental changes in systems for fear and distress across puberty (including the effects of the social environment), that could explain clinical data indicating that adolescent anxiety disorders often precede depression.

Environmental aspects. The central nervous system is exquisitely sensitive to interactions with various elements of its environment virtually from the moment of conception. The social and physical environment comprises sources of both risk and protection for many different disorders occurring at all points along the life span, and methods for studying such phenomena as gene expression, neural plasticity, and various types of learning are rapidly advancing. As with developmental aspects, environmental influences may thus be considered as another critical dimension of the RDoC matrix. The effects of a particular interaction with the environment, e.g., the effects of early child abuse, may pose risk for a wide variety of disorders. As another example, illicit drug use may cause sensitization of mesolimbic dopamine circuits that generalizes to other drugs of abuse and addictive behaviors. Thus, it is hoped that a research program organized around the relevant circuit-based dimensions that are affected, independent of a particular disorder, will accelerate knowledge regarding such environmental influences along the entire range of analysis from genes to behavior.

Discussion

1. As mentioned above, the current organization is focused on (and constrained by) circuit definitions in order to (1) avoid an over-specification and proliferation of constructs, and (2) provide an organizing point that facilitates the integration both of genetic, molecular, and cellular levels of analysis regarding sub-components of circuits, and of behavioral and self-report levels of analysis regarding the kinds of behaviors that circuits implement. The intent is not to arbitrarily exclude constructs, but rather to foster thinking about how constructs are related at various levels of analysis. For example, extraversion is not listed in the draft matrix, but might be considered to represent another aspect of social dominance -- in that they are both typically described in terms of activity in mesolimbic dopamine systems, and thus may reflect different aspects of what is fundamentally the same dimension.
2. The framework is directed toward constructs most germane to mental disorders, and makes no

claim to span the entire gamut of functional behavior. For instance, circuits relevant to thermoregulation and reproductive behavior are not included.

3. The number of constructs might well be viewed as sparse by many scientists. The attempt has been to include relatively high-level constructs in order to avoid an over-specification of functions that could become unwieldy and also necessitate unnecessarily frequent revisions to the list as research progresses. However, the framework is meant to foster, not discourage, research that explicates mechanisms within and across the constructs as listed. As stated above, the current framework should be viewed as a starting point and part of a work in progress.
4. The complexity of the brain is such that circuits and constructs will necessarily have considerable overlap, and arbitrary separations are unavoidable. For instance, the basolateral amygdala is well-known to be involved with both threat and appetitive processing. This reflects the hierarchical nature of the nervous system, and the difficulty of creating a system that encompasses various levels in one framework. It should also be noted that some constructs, such as emotional regulation or homeostasis, are not listed here; these are considered superordinate principles of nervous system activity that operate across many different circuits.
5. Research with post-mortem tissue samples may be appropriate for studies within the RDoC framework, where the hypotheses and other variables are conceived in terms of relevant domains and constructs.
6. The RDoC framework is explicitly agnostic with respect to current definitions of disorders. For instance, depression as a clinical syndrome has been related to abnormal activity in the amygdala, anterior cingulate cortex, nucleus accumbens, and multiple monoamine systems, while also strongly comorbid with multiple anxiety disorders, eating disorders, etc. The idea is that studying the individual mechanisms may lead to better understanding of current disorders, or perhaps new and novel definitions of disorders, but in either case improved information about treatment choices.
7. As mentioned above, the aim of RDoC is to create a framework for grouping participants in research studies, in order to create a foundational research literature that informs future versions of nosologies based upon genetics and behavioral neuroscience. RDoC is **not** intended for clinical diagnosis at the current time. In the future, research supported by RDoC could inform diagnostic approaches using new laboratory procedures, behavioral assessments, and novel instruments to provide enhanced treatment and prevention interventions. It is also hoped that RDoC will support enhanced development of new pharmacological and psychosocial interventions based upon neurobiological and behavioral mechanisms.

Process and Final Product

The NIMH intends that the RDoC process be as transparent as possible. An internal NIMH steering group, advised by a small group of external experts, has created the initial RDoC framework and devised the list of candidate domains, constructs, and classes of variables. NIMH issued a companion Request for Information (RFI) in the NIH Guide to seek input about all aspects of this first draft of the RDoC matrix and process. These comments were taken into account in further refining the initial version of the matrix.

A series of workshops is currently in progress as an initial step in defining the specifications for each construct. At a minimum, one workshop will be held for each of the five domains. However, in order to gain experience with the process, the first workshop focused on the construct of working memory. Each workshop involves experts from various areas that span the RDoC's units of analysis. Participants are asked to discuss and decide upon current findings, paradigms, and procedures relevant to each level of analysis, along with critical research questions. Proceedings of each workshop are posted on the RDoC page of the NIMH web site for continuing commentary and suggestions for changes. Depending on the nature and extent of comments, a second workshop may be held to achieve consensus on final specifications.

The final specification for each construct will consist of:

1. A definition of the construct's functional aspects, summary of relevant circuitry, and relationship to other constructs;

2. A list of current state-of-the art measures, paradigms, and procedures at each level of analysis;
3. Current pressing research questions and issues pertaining to the construct, including one or two salient examples of the groupings of DSM/ICD categories that might be included in studies addressing these questions.

The intent of the RDoC is to accelerate the pace of new discoveries by fostering research that translates findings from basic science into new treatments addressing fundamental mechanisms that cut across current diagnostic categories. The research specifications are intended to guide investigators in conducting such integrative research by including cutting-edge variables in research applications. However, since RDoC is a research framework, use of such variables is not required; indeed, one goal is to speed the pace of new information at all levels of analysis. For this reason, RDoC will incorporate a mechanism for continual evaluation of new findings, and inclusion into the domain/construct specifications. While the exact procedures remain to be worked out, it is anticipated that the NIMH steering group will work together with subject-area experts from each of the relevant domains to accept nominations (from the evaluation team or from scientists in the field) for modifications and additional listings.

Although the formal period for commenting under the RFI has terminated, NIMH welcomes continuing commentary regarding any aspect of the RDoC project, including, but not limited to, the following points. Comments may be emailed to **rdoc@mail.nih.gov**.

1. The overall RDoC framework, including the organization of the Domains and Constructs, and the Units of Analysis.
2. Particular constructs that should be added, deleted, merged, or changed.
3. Criteria for determining what constructs should be included or modified.
4. “Grain size” of the constructs.
5. Criteria for making changes to the domain and construct specifications.

NIMH staff look forward to working with all groups of interested stakeholders as the RDoC project is developed.

The National Institute of Mental Health Strategic Plan

Released August 2008

NIMH Vision

NIMH envisions a world in which mental illnesses are prevented and cured.

NIMH Mission

The mission of NIMH is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery and cure.

For the Institute to continue fulfilling this vital public health mission, it must foster innovative thinking and ensure that a full array of novel scientific perspectives are used to further discovery in the evolving science of brain, behavior, and experience. In this way, breakthroughs in science can become breakthroughs for all people with mental illnesses.

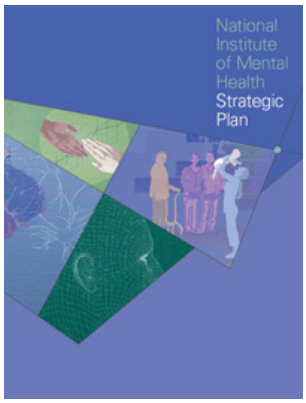
In support of this mission, NIMH will generate research and promote research training to fulfill the following four objectives:

- Promote discovery in the brain and behavioral sciences to fuel research on the causes of mental disorders
- Chart mental illness trajectories to determine when, where, and how to intervene
- Develop new and better interventions that incorporate the diverse needs and circumstances of people with mental illnesses
- Strengthen the public health impact of NIMH-supported research

The National Institute of Mental Health Strategic Plan

Envisioning a world in which mental illnesses are prevented and cured

NIMH Strategic Plan



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Strategic Research Priorities

Director's Message

The National Institute of Mental Health (NIMH) has just entered its seventh decade as the nation's scientific leader in the fight against mental illness. The landscape of mental health research has changed considerably over these decades. A critical acceleration began in the 1970's and 1980's when researchers began making rapid strides toward understanding the science of human behavior and the ways in which medicines can be used to treat illnesses. In the 1990's, the "Decade of the Brain" yielded insights into fundamental aspects of how the brain works including new ways of visualizing the brain with imaging technologies. This era also led to advanced methods for studying the interaction between the brain, behavior, and the environment. These advances, in turn, have set the stage for the current era which might be called the "Decade of Discovery." Many of the scientific opportunities in this discovery era were scarcely imagined 10 years ago. For NIMH to continue fulfilling its vital public health mission, the Institute needs to remain adaptive and explore fully the changing scientific landscape, ensuring that breakthroughs in science become breakthroughs for people with mental disorders.

When scientists think about this changing landscape, we usually focus on new and novel technologies and innovative models for approaching science. New maps and new mapping tools for the human genome, for instance, have transformed our understanding of how individuals genetically vary from each other and how these variations can put some people at increased risk for certain illnesses. Neuroimaging tools to visualize the brain have given us an unprecedented view of brain activity, providing a new understanding of its development and a picture of how specific networks of cells change with experience. One goal of this Strategic Plan is to translate these and other advances to what the National Institutes of Health (NIH) calls the "4 P's" of research: increasing the capacity to *Predict* who is at risk for developing disease; developing interventions that *Preempt* (or interrupt) the disease process; using knowledge about individual biological, environmental, and social factors for *Personalized* interventions; and ensuring that clinical research involves *Participation* from the diversity of people and settings involved in health care.

It is important to note that the changing landscape is found outside scientific laboratories as well. Demographically, America is a different nation than it was 10 years ago: we are more diverse, we are aging, and we are increasingly challenged by the costs and complexities of health care. A major goal of this Strategic Plan is to enhance the impact of research on the enormous public health burden that mental illnesses have across the lifespan. Our success cannot be measured solely by our traditional "outputs": the numbers of grants, papers, or discoveries supported. In addition, NIMH must measure success by "outcomes": how well the research we support provides the evidence base for mental health care providers to preempt illness for those at risk (including prevention targeted to those individuals most at risk), enhance recovery for those affected, serve diverse and previously under-served populations, and reduce premature mortality among persons with mental illness.

The urgency of this cause cannot be over-stated. The President's New Freedom Commission on Mental Health, which examined the need for reform of the mental health care system, concluded that the problems of fragmentation, access, and quality of mental health care were so great that nothing less than transformation would suffice. With several large-scale clinical trials completed by NIMH, we can add that for too many people with mental disorders even the best of current care is not good enough. To fully address these issues, we must continue to (a) discover the fundamental knowledge about brain

and behavior and (b) use such discoveries to develop better tools for diagnosis, preemptive interventions, more effective treatments, and improved strategies for delivering services for those who provide direct mental health care. These activities point toward NIMH's ultimate goal, which is not merely to reduce symptoms among persons with mental illness, but also to promote recovery among this population and tangibly improve their quality of life.

There is an unavoidable tension between the urgent need for transformation and the longer-term nature of scientific progress. Scientific progress is generally slow and incremental—too slow and too incremental for families who need more effective treatments today. Yet, progress has been made and it has been accelerating over the past decade. This Plan is our commitment to continue the accelerated pace of scientific progress by generating, over the next 5 years, the best mental health research that will have the greatest public health impact and continue to fuel the transformation of mental health care.

Thomas R. Insel, M.D.
Director, NIMH

NIMH Vision

NIMH envisions a world in which mental illnesses are prevented and cured.

NIMH Mission

To transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.

Introduction:

As the lead Federal agency for research on mental and behavioral disorders, the National Institute of Mental Health (NIMH) envisions a world in which mental illnesses are prevented and cured.

In consideration of this vision, the mission of NIMH is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. The burden that this research addresses is enormous. In a given year, an estimated 13 million American adults (approximately 1 in 17) have a seriously debilitating mental illness.[1, 2] Mental health disorders are the leading cause of disability in the United States and Canada, accounting for 25 percent of all years of life lost to disability and premature mortality (Disability Adjusted Life Years or DALYs).[3] Moreover, suicide is the 11th leading cause of death in the United States, accounting for the deaths of approximately 30,000 Americans each year.[4] Schizophrenia, bipolar disorder, depression, post-traumatic stress disorder, eating disorders, autism, and other disorders are serious, often life-threatening, illnesses for which we need reliable diagnostic tests, new treatments, and effective strategies for prevention.

This public health mandate demands that we harness powerful scientific tools to achieve better understanding, treatment, and ultimately, prevention of these disabling conditions. To fulfill its mission, the Institute:

- Conducts research on mental disorders and the underlying basic science of brain and behavior.
- Supports research on these topics at research settings throughout the United States and the world.
- Collects, analyzes, and disseminates information on the causes, occurrence, and treatment of mental illnesses.
- Supports the training of more than 1,000 scientists each year to carry out basic and clinical mental health research.
- Communicates with scientists, patients, the news media, and primary care and mental health professionals about mental illnesses, the brain, behavior, and opportunities and research advances in these areas.

Important discoveries in areas such as genetics, neuroscience, and behavioral science largely account for the substantial gains in knowledge that have helped us to understand the complexities of mental illnesses and behavioral disorders over the past 15 years. The elaboration of observed behavior, which includes such aspects as cognition, emotions, social interactions, learning, motivation, and perception, are the observable “tips of the iceberg” in reflecting the expanse of complexity further revealed in studying genes, proteins, cells, systems, and circuits. To inspire and support research that will continue to make a difference for those living with mental illness, and ultimately promote recovery, we developed this Strategic Plan to guide what has become an increasingly complex research effort (see Appendix A for details on the strategic planning process). The Plan seeks to bring into sharper focus questions and perspectives that will transform the diagnosis, treatment, and prevention of mental disorders.

With this goal in mind, NIMH identified four overarching Strategic Objectives:

Promote Discovery in the Brain and Behavioral Sciences to Fuel Research on the Causes of Mental Disorders
Chart Mental Illness Trajectories to Determine When, Where and How to Intervene
Develop New and Better Interventions that Incorporate the Diverse Needs and Circumstances of People with Mental Illnesses
Strengthen the Public Health Impact of NIMH-Supported Research [5]

The four Strategic Objectives can be viewed as a cumulative progression of the Institute’s priorities for the next 5 years. This strategy begins with promoting discovery in the brain and behavioral sciences in order to better understand the workings of the brain that can be translated to the study of mental disorders. In effect, our efforts to understand how changes in the brain can lead to mental illness will inform (and be informed by) fundamental research to understand the trajectories of mental illnesses across the lifespan and across diverse populations. By learning more about the trajectories by which mental illnesses develop, we hope to stimulate innovative psychosocial and biomedical approaches that can preempt or change these trajectories before mental illness occurs. Finally, we will retain a strong focus on public health impact and create better methods for ensuring that our research reaches all whose lives are affected by mental illness, as well as those who are dedicated to their care.

It is important to also highlight several core research themes that are essential to advancing and accomplishing the Strategic Objectives. First, in order for research on mental disorders to more fully harness the scientific power of brain-behavior science, sound efforts must be made to redefine mental disorders into dimensions or components of observable behaviors that are more closely aligned with the biology of the brain. Such an effort will result in a research-based description of the key elements of mental disorders, providing even greater traction on the potential mechanisms that can cause mental suffering and targets for more effective preemption and treatment.

Second, it is imperative that NIMH continue to lead efforts that foster data and resource sharing. As we strive to capture and understand the complexity of mental disorders, the data and resources generated by our research also entail greater complexity and diversity. We are committed to working with the scientific community to support the broad sharing of data and the resources necessary to accelerate scientific progress

Third, all advances rest on our ability to support and train future generations of mental health scientists. Future research scientists will use different neurobehavioral, clinical, and services skill sets as the field advances and transforms itself across traditional academic boundaries. It is equally clear that training must inspire creativity, innovation, and a thirst to make a difference in the lives of those with mental disorders. Balancing these needs and finding improved ways to mentor and train the most talented young researchers are fundamental to the future of mental health research. For this reason, the National Advisory Mental Health Committee (NAMHC) is developing a separate document that will outline the Institute’s future research training priorities.

Based on these three research themes, the Strategic Objectives and underlying strategies outlined in this document serve as a guide to the Institute for advancing mental health science and ensuring that research-based interventions and information are made widely available. They also seek to complement the President’s New Freedom Commission on Mental Health report by outlining new research-based tools for transforming the mental health services provided by partner Federal agencies, particularly

those of the Substance Abuse and Mental Health Services Administration (SAMHSA).[6] Ultimately, this Strategic Plan represents NIMH's commitment to studying and providing the research evidence that can be used to transform the treatment of mental disorders, paving the way for prevention, recovery, and cure.

Strategic Objective 1: Promote Discovery in the Brain and Behavioral Sciences to Fuel Research on the Causes of Mental Disorders.

We will support basic, translational, and clinical research to gain a more complete understanding of the genetic, neurobiological, behavioral, environmental, and experiential factors that contribute to mental disorders.

This is a time of great scientific excitement in mental health research. Building on new discoveries from genetics, neuroscience, and behavioral science, we are better poised to understand how the brain, behavior, and the environment interact to lead to mental disorders. Mental illnesses are now studied as brain disorders, specifically as disorders of brain circuits. The current era of neuroscience promises to reveal much about their origins, development, and manifestations. In addition to translating neuroscience discoveries to the clinic, we are also in a phase of using clinical findings (e.g., genetic or brain imaging data) from those with mental disorders to guide research on neurobiology.

Research has made significant progress in identifying a wide array of the genetic, neurobiological, and behavioral components that comprise mental disorders. For example, studies have shown that certain genetic variations can increase risk for developing a mental disorder. Environmental and experiential influences, such as traumatic stress, may interact with specific genetic variations during sensitive periods of development. This complex interaction between genetics, environment, experiences, and development may compound risk for mental disorders by altering the structure and function of neural pathways relevant to some forms of adaptive behavior.

With new insights come new challenges. It is becoming increasingly clear that the genetic underpinnings of mental disorders are highly complex, likely involving the interaction between many risk genes. An enormous variety of experiences and environmental factors may influence development, and the ability of these factors to confer risk may change across the lifespan. It is challenging to demonstrate how interactions between genes, environment, experiences, and development contribute to the formation and function of neural circuits. We still know little about how information is stored in neural circuits. In addition, the very definition of mental disorders as complex clusters of behaviors makes it difficult to deconstruct behavioral components and link them to underlying neural circuitry.

Improving our understanding of the underlying causes of mental disorders will provide the necessary foundation for better diagnosis and interventions. To clarify and integrate these neurobiological, behavioral, environmental, and experiential components, NIMH will engage in a number of strategies:

Strategy 1.1: Develop an integrative understanding of basic brain-behavior processes that provide the foundation for understanding mental disorders.

To further clarify how changes in neural activity contribute to mental disorders, it will be necessary to know more about the basic neuroscience of neural circuit formation and how these circuits interact to contribute to observable behaviors. These efforts will require teams to integrate findings from studies of genomics, neuroscience, behavior, and the environment. This research will serve as the foundation for translation to clinical studies. To facilitate these discoveries, NIMH will:

Support research to improve our basic understanding of the development, structure, and function of neural circuits, with a focus on those most relevant to mental disorders.

Determine the mechanisms and course of brain development and how this development maps

onto or is affected by observable changes in behavior.

Determine the mechanisms by which genes and their products (e.g., signaling molecules, proteins, peptides, hormones) influence the development and functioning of neural cells and circuits across the lifespan.

Define the mechanisms by which environmental and experiential influences (e.g. prenatal-postnatal exposure to toxins, traumatic stress, social interaction) affect the development and functioning of neural cells and circuits.

Develop novel tools and methodologies for understanding how populations of neural cells work together within and between brain regions. For example, develop:

Improved methods for recording cellular activity

Mathematical modeling of cellular and circuital functioning

New ways of imaging intracellular communication

Promote discovery of novel risk/susceptibility genes (including transcription factors, non-coding regulators of gene expression, and proteins) to understand:

Their function in cells, circuits, and systems

How these risk/susceptibility genes impact behavior

How environmental and experiential influences interact with susceptibility genes to compound risk

Strategy 1.2: Identify the genetic and environmental factors associated with mental disorders.

Research has demonstrated that genes exert a significant influence on the risk for many disorders, including autism, schizophrenia, and bipolar disorder. However, studies are further revealing the complexity of the genetic, behavioral, experiential, and environmental factors that contribute to mental disorders. A single disorder might result from the interaction of combined, small effects of many different genetic variations, none of which is powerful enough to cause the disorder by itself. Alternatively, it is possible that a disorder might result from diverse, single gene mutations that result in similar physiological changes. Additional research will help ascertain whether a specific gene variation contributes to the cause of a disorder, a subgroup within a disorder, or a symptom that might be shared across multiple disorders. With the sequencing of the human genome, improved understanding of how genes are expressed, and new technologies to measure variation in the genome, we have an unprecedented opportunity to define how genes confer risk for the major mental disorders, potentially yielding new diagnostic and therapeutic targets.

Genes appear to explain only part of the risk for developing these disorders. Research has also demonstrated the importance of environmental and experiential factors in conferring risk for many mental disorders. These factors vary in scope and complexity, ranging from exposure to toxic substances *in utero* to social and family circumstances. Due to this wide variation, environmental and experiential influences are challenging to define and measure. In addition, some experiential influences, such as stress, may be risk factors for multiple disorders.

Epigenetic mechanisms—ways that the environment influences genes to control their function—will likely prove very important in the cause of these complex disorders. To add to this complexity, it is likely that the interplay between genes and the environment changes over the lifespan. To improve identification of the genetic and environmental factors associated with mental disorders, we will:

Define genomic variations associated with mental disorders.

Apply current and emerging technologies to identify how variations in the sequence of the genome and its packaging within the cell may be associated with susceptibility and resistance to mental disorders.

Continue to develop large scale repositories (e.g., the NIMH Center for Collaborative Genetic Studies on Mental Disorders) as resources of biological samples, phenotypic data, and genotypic data for broad use by the international scientific community in its search for the genetic basis of mental disorders.

Develop statistical theory and methods to model and detect the role of genomic variation in the

development of mental disorders.

Determine the biological consequences of genomic variations associated with mental disorders.

Identify how variations within the genome influence the expression of those genes and the function of the encoded proteins to alter cells, circuits, and behavioral outcomes.

Ensure access to cell lines and model organisms to demonstrate how changes in gene sequence may change the function of the resulting protein.

Determine how environmental and experiential influences interact with genes to identify mechanisms by which experience confers enduring changes in gene expression.

Improve methods for defining and measuring the diverse types of environmental and experiential influences in both human and non-human animal studies.

Develop and apply tools for epigenetic research to determine how, when, and where experience affects gene expression.

Ensure that clinical studies on epigenetic mechanisms include samples from diverse populations (e.g., race, ethnicity, age, sex).

Examine how known sensitive periods across the lifespan may be possible points of vulnerability or resilience for gene-environment interactions.

Continue to support studies of plasticity and resiliency of the nervous system across the lifespan.

Strategy 1.3: Identify and integrate biological markers (biomarkers) and behavioral indicators associated with mental disorders.

Biomarkers are biological indicators of a physiological or disease process. Examples of biomarkers can include genetic mutations, altered levels of a specific protein in blood or spinal fluid, and brain abnormalities observed in neuroimaging tests. Detecting biomarkers may predict risk for developing a mental disorder or may aid in the identification, diagnosis, and treatment of individuals with the disorder. Currently, very few biomarkers have been identified for mental disorders due in part to their complexity and an incomplete understanding of the neurobiological basis of mental disorders. Mental disorders also have observable behaviors associated with them (e.g., startle reactions, compulsions, social avoidance) that, like biomarkers, once identified can indicate a possible underlying disorder and assist mental health professionals with proper diagnosis and treatment. To accelerate the identification of biomarkers and behavioral indicators for mental disorders, it will be important to:

Support the development of integrated profiles/panels of clinically relevant and validated biomarkers and behavioral indicators (e.g., genes, proteins, brain images, behaviors, or a combination), creating “biosignatures” of disorders. A single biomarker is not likely to be sufficient to indicate the presence of a disorder, but a combination of biomarkers and behavioral indicators of small effect might. For example, a biosignature could consist of a genetic variant, an abnormal amount of a certain protein, a distinct neuroimaging pattern from a brain scan, a certain response during a cognitive test, or any number of indicators from blood, sweat, or other biological fluids.

Support studies to identify biomarkers and behavioral indicators for different stages of illness and recovery (e.g., biomarkers for onset vs. relapse, biomarkers indicating risk vs. resilience).

Support research that examines biomarkers that may be common to mental disorders and other medical disorders (e.g., inflammatory markers for heart disease) in order to identify shared molecular pathways that contribute to development of mental disorders.

Strategy 1.4: Develop, for research purposes, new ways of classifying mental disorders based on dimensions of observable behavior and neurobiological measures.

Currently, the diagnosis of mental disorders is based on clinical observation—identifying symptoms that tend to cluster together, determining when the symptoms appear, and determining whether the symptoms resolve, recur, or become chronic. However, the way that mental disorders are defined in the present diagnostic system does not incorporate current information from integrative neuroscience

research, and thus is not optimal for making scientific gains through neuroscience approaches. It is difficult to deconstruct clusters of complex behaviors and attempt to link these to underlying neurobiological systems. Many mental disorders may be considered as falling along multiple dimensions (e.g., cognition, mood, social interactions), with traits that exist on a continuum ranging from normal to extreme. Co-occurrence of multiple mental disorders might reflect different patterns of symptoms that result from shared risk factors and perhaps the same underlying disease processes.

To clarify the underlying causes of mental disorders, it will be necessary to define, measure, and link basic biological and behavioral components of normal and abnormal functioning. This effort will require integration of genetic, neuroscience, imaging, behavioral, and clinical studies. By linking basic biological and behavioral components, it will become possible to construct valid, reliable phenotypes (measurable traits or characteristics) for mental disorders. This will help us elucidate the causes of the disorder, while clarifying the boundaries and overlap between mental disorders. In order to understand mental disorders in terms of dimensions and/or components of neurobiology and behaviors, it will be important to:

Initiate a process for bringing together experts in clinical and basic sciences to jointly identify the fundamental behavioral components that may span multiple disorders (e.g., executive functioning, affect regulation, person perception) and that are more amenable to neuroscience approaches.
Develop reliable and valid measures of these fundamental components of mental disorders for use in basic studies and in more clinical settings.
Determine the full range of variation, from normal to abnormal, among the fundamental components to improve understanding of what is typical versus pathological.
Integrate the fundamental genetic, neurobiological, behavioral, environmental, and experiential components that comprise these mental disorders.

Sidebars: Strategic Objective 1

1. Beyond Nature vs. Nurture

Genomics has become central to biomedical research, yet genes may explain only a piece of the risk for developing a disorder. While rare, single gene mutations are at the root of hereditary disorders, such as cystic fibrosis and Huntington's disease, most mental disorders are not caused by mutations in one gene. Rather, these disorders are "complex" or polygenic—meaning that they are associated with variations in multiple genes, likely in combination with environmental and experiential factors. Genetic variations are not the sole "cause" of the disorder; they increase risk by changing proteins, cells, and circuits important for behavior and cognition. Already we can see how differences in genetic sequence are associated with differences in brain circuits or brain function, even in people who do not have a disorder. One challenge for the next 5 years will be explaining the mechanisms by which these genomic differences lead to variations in cells and circuits with resulting changes in behavior or cognition. Another challenge will be explaining the non-genomic risks for developing a disorder.

In the past, the debate has been between nature (genetics) and nurture (environment) as causes of mental disorders. Today we recognize the complex interplay between nature and nurture by asking: how does experience interact with biological susceptibility to increase risk or resilience? For example, certain experiences, such as childhood maltreatment, may interact with a person's genetic vulnerability, increasing the risk for developing PTSD or depression in adulthood.[7] , [8] Other influences, such as receiving positive social support, may offset the negative effects of these risk genes and can buffer against developing a mental disorder later in life.[9]

Understanding the mechanisms by which our experiences are integrated into our biology will rely largely on the developing field of epigenetics—the study of how environmental influences regulate gene expression. Our DNA is decorated with protein complexes that modify how and when genes are expressed. Experiences, such as traumatic stress, do not alter the DNA sequence but can modify these protein complexes, leading to either enhanced or silenced expression of specific genes. Epigenetic modifications may provide the platform through which the environment interacts with the genome,

serving as a means for learning and adaptation. Critical issues for future studies of gene-environment interactions will be to define the range of environmental exposures (e.g., maternal environment, infections, toxins, stress, social interaction) that might affect the genome throughout life and to determine how environmental factors are translated into changes in gene expression. These studies will trace the imprints of experience on our DNA, revealing, perhaps years later, how nature and nurture are entwined.

2. Tracing the Brain's Circuitry

The human brain has approximately 100 billion neurons connected through complex networks, making it extremely challenging to trace the brain's wiring plan. However, by combining innovative visualization approaches, we may better understand how these circuits interact physically and functionally. Perhaps the most important breakthroughs have come from new techniques for studying neural circuits.

One way to follow neuronal connections is to label the neurons with fluorescent probes. Until recently, however, these probes have been limited to a handful of colors, restricting the number of neurons that can be discerned at one time. A new genetic method labels neurons in mice with a rainbow of fluorescent shades. Instead of teasing out the wiring of the brain by one or two cells at a time, this new technique, called "Brainbow", provides the means for tracing whole populations of neurons at once.[10]

In another advance, neuroscientists have genetically modified neurons to express light-activated proteins—named ChR2 and NpHR—found in certain light-responsive algae and bacteria.[11, 12] These neurons can be turned on and off with different colors of light, allowing scientists to manipulate an entire cell-defined circuit in a behaving animal.

While studies in humans lack the cellular precision of studies in mice, diffusion tensor imaging (DTI) maps the paths and directions of neuronal fibers (white matter) responsible for long-distance communication between regions of the human brain. A recent application of DTI has uncovered abnormal wiring in the brains of people with Williams Syndrome, a rare genetic neurodevelopmental disorder.[13] The researchers suspect the abnormalities result from neurons migrating to the wrong destinations during development.

These new techniques, whether in mice or humans, should provide insight into how abnormal wiring may give rise to brain disorders. Increasingly, to understand the neural basis of mental disorders, we will be combining techniques that integrate across levels of functioning—from cells to circuits to behavior.

Strategic Objective 2: Chart Mental Illness Trajectories to Determine When, Where, and How to Intervene.

We will chart the course of mental disorders over the lifespan in order to understand ideal times and methods for intervention to preempt or treat mental disorders, and hasten recovery.

Mental disorders are a group of chronic, changing conditions. The symptoms often begin to appear in childhood and adolescence and ebb and flow over the course of an individual's life. Research demonstrates that the symptoms of many medical disorders (e.g., Parkinson's, Alzheimer's, coronary artery disease) represent a late stage of a process that began years earlier. As with many other medical illnesses, science promises to redefine mental disorders along a trajectory moving across stages of risk: from early symptoms, to full symptoms or syndromes, to remission, relapse, and recovery. NIMH aims to compare trajectories of healthy development to those of mental disorders in order to better understand the first instance or instances when development moves off course. Doing so will allow us to pinpoint the best times and techniques to preempt the onset of symptoms or halt and reverse the progression and recurrence of illness. By predicting, detecting, and intervening early in the disease process, we can dramatically improve an individual's likelihood of a life without suffering from a mental disorder.

Charting the course of mental disorders requires attention to genetic, neurobiological, behavioral,

experiential, and environmental factors that confer a risk of developing a mental disorder. Individual characteristics, such as age, sex, race, ethnicity, culture and socioeconomic background, are critical considerations in this research. Either singly or in combination, these different factors and characteristics may not only increase the likelihood an individual will develop a mental disorder, but also affect how well that person will respond to interventions and his or her tendency to experience adverse side effects. The results of these efforts will enable NIMH to foster more personalized, preemptive, and effective therapeutic interventions.

To advance research on the trajectories of mental illnesses across the lifespan, NIMH will undertake the following strategies:

Strategy 2.1: Define the developmental trajectories of mental disorders.

Genetic variation interacts with experiential and environmental factors dynamically, varying across stages of development. We can view mental disorders as following trajectories throughout the lifespan, beginning with risk and evolving as symptoms or syndromes, which in turn can follow cycles of remission and relapse. Our challenge is to redefine disorders by understanding them as unfolding developmental processes, recognizing that these disease processes can have different consequences at different life stages. To understand the origin and development of mental disorders, we need a firm understanding of how normal brain development shapes behavior as well as how experience, in turn, shapes brain development. In support of this effort, NIMH will:

- Determine how periods of change in development (e.g., infancy to young childhood, childhood to adolescence, adolescence to adulthood, adulthood to old age) may also be periods of vulnerability for the emergence of risk, symptoms, remission or relapse.
  - Augment descriptive studies of developmental changes in behavior, hormone levels in the brain and body, brain volume, etc. with studies of how these changes affect an individual's genes, molecules, and cells, including neural cells.
  - Link studies of brain development with behavioral development to understand how brain regions critical for mental disorders are associated with typical and atypical behavioral functioning.
- Broaden the study of biomarkers and biosignatures of disorders to include not only ways to detect genetic, neural, and/or behavioral markers for deviation from a healthy course of development and for risk or onset of disorder, but also ways to indicate illness onset, progression, relapse, remission, and recovery.

Strategy 2.2: Enhance understanding of how cultural diversity may influence the developmental trajectories of mental illness.

We will enrich the types of data used in the study of mental illnesses to enable more thorough and precise analyses of cultural and ethnic factors that may be involved in risk, resilience, and recovery from illness.

- When identifying behavioral, neural, and/or genetic markers along the trajectory of illness, design the studies to consider variation in relation to age, sex, gender, race, ethnicity, and other important socio-demographic factors.
- Ensure and enhance diversity in creating and supporting data and resource repositories, such as the NIMH Genetics Repository. This may include, for example, international populations and isolated cases.
- Examine how genetic, environmental, experiential, societal, and behavioral differences associated with diverse ethnic and cultural groups may affect how well interventions preempt or treat illnesses, and enhance recovery.

Strategy 2.3: Develop tools to better define and identify risk and

protective factors for mental illness across the lifespan.

An understanding of the developmental trajectory of illnesses opens the possibility that we could intervene and alter trajectories, thereby preempting suffering associated with disease. By using the example of efforts in other fields of medicine that have adopted this approach (e.g., cardiology with regard to coronary artery disease), we will facilitate research to identify risk at the individual level (as opposed to population level) and to develop a new set of interventions. To develop such tools and methods to intervene in the trajectory of illness, NIMH plans to:

Identify malleable and robust risk factors for different phases of the disease trajectory. Factors would span across genes, cells, systems, behaviors, emotions, social interactions, and the environment to understand their contribution in pre-symptomatic stages of mental illness, onset, relapse, and recovery. This knowledge would be used to develop integrated risk checklists, covering neurological, behavioral, social, and environmental factors, including exposure to stress and both psychological and physical trauma, so that we can describe patterns of risk at an individual level.
Develop and test innovative interventions based on robust risk factors to reduce risk and positively alter trajectories of illness.
Identify predictors (e.g., biological, genetic, behavioral) of intervention response and side effects in different patient populations, throughout the life course, throughout the trajectory of illness, and throughout the clinical research and drug development pipelines.

Sidebars: Strategic Objective 2

1. Mapping the trajectory of mental disorders using imaging technologies

Recent longitudinal studies have mapped the patterns of brain development in healthy youth and in those with mental illness. The results of these studies will guide us as we chart the initiation and progression of mental illness across the lifespan, further clarifying pathways for intervention. Although some loss of neurons and their connections is normal as the brain matures, adolescents with childhood onset schizophrenia show four times the normal rate of gray matter loss in the front of the brain.[14] By contrast, children with bipolar disorder show a more complicated pattern of gray matter gains in areas in the left hemisphere and losses in the right hemisphere, and in mood regulating circuitry in the mid-front part of the brain.[15] Pediatric bipolar disorder and childhood onset schizophrenia appear to involve different underlying neural circuits, even though the two illnesses share some symptoms and several genetic risk factors. Meanwhile, youth with attention deficit hyperactivity disorder (ADHD) have delayed patterns of brain maturation—three years in some regions, on average.[16] The delay in ADHD is most prominent in the frontal lobe, important for the ability to control thinking, attention, and planning.

2. Early detection of risk factors for mental disorders

Early detection of risk factors for illnesses leads to early intervention, which can make all the difference in the quality of life of affected individuals and their families. Recent research has shown that about half of children with autism spectrum disorders (ASD) can be diagnosed soon after their first birthday, while others with the disorder may appear to develop normally until that age and then regress during their second year.[17] In the past, clinicians were rarely able to diagnose ASD before age three, potentially missing the most important period for intervention. Building upon these new findings, NIMH envisions criteria that clinicians can use to diagnose ASD in one-year-olds with the potential for recovery by age three.

Following a different trajectory, the psychotic phase of some mental illnesses emerges when an individual is in their late teens or early twenties. In recent work, NIMH-funded researchers have been able to detect illnesses like schizophrenia in up to 80 percent of youth who will develop the disorder (median age of 16) well before the emergence of psychosis.[18] Knowing these risk factors — particularly

combinations of them—could help clinicians detect and treat schizophrenia years before the psychotic phase with the potential of avoiding or, at least forestalling, the most disabling part of the illness.

Strategic Objective 3: Develop New and Better Interventions for Mental Disorders that Incorporate the Diverse Needs and Circumstances of People with Mental Illness.

We will improve existing approaches and devise new ones for the prevention, treatment, and cure of mental illness, allowing those who may suffer from these disorders to live full and productive lives.

The rapid discovery rate for new factors affecting the trajectories of illness suggests that new targets for psychosocial and biomedical interventions should be examined in a systematic way. We need new and better methods to intervene at all points along the trajectories of mental illnesses to preempt the occurrence of disease or, when that is not possible, to hasten recovery.

Traditionally, intervention research, whether preventive or therapeutic, has focused on the absence or reduction of symptoms of mental illness. Alleviating symptoms, although important, does not necessarily address the totality of a person's life, including how well he or she functions in their community and workplace. While an intervention may potentially prevent or alleviate the symptoms of a mental illness, there is also the possibility that it may not help; in some cases it might even further impair a person's ability to function in everyday life. Moreover, an effective preventive strategy or treatment regimen may prove to be too difficult or expensive for proper use by providers. Intervention research, then, must emphasize efficacious recovery as its ultimate goal.

In general, traditional intervention research has focused on comparing how groups of individuals receiving an experimental intervention fare against a comparison group that does not receive that intervention. This approach has given us information about treatments for selected groups of people but not necessarily about how to choose the best treatment for a specific individual. We need personalized medicine: tailoring pharmacological, behavioral, and other forms of treatment to the needs of each individual. A new generation of clinical trials is needed to gather a wider array of data and examine the kinds of questions that can be used for personalized decision-making in medicine.

We need innovative approaches to help providers of mental health interventions ensure that every person who may fall along the trajectory of mental disorder can be helped to preempt or recover from illness. To do so, we will broaden our concept of intervention research to address how these interventions affect an individual's ability to live a full life, as well as the impact on the providers and settings in which the interventions are delivered (e.g., medical settings, schools). We will also need to address relationships between mental disorders and other illnesses, such as substance abuse and heart disease. In addition to shifting the intervention focus to treating the whole person, it provides substantial opportunity for the reduction of mental illness-related mortality. Ultimately, our intervention research will focus on new targets, resulting in preventive and treatment strategies that allow individuals and their families, their health providers, and their social support systems to find the means to preempt or stop the progression of mental illness.

To further develop interventions that are personalized and work in multiple and diverse settings such as clinical practices, hospitals, schools, and communities, NIMH will employ the following strategies:

Strategy 3.1: Further develop innovative interventions and designs for intervention studies.

The body of work in mental health intervention research is vast and has led to numerous advances in the prevention and treatment of mental disorders. Future research needs to build on this existing scientific knowledge. Additionally, we must adopt innovative approaches to develop personalized preventive and therapeutic approaches for those in need.

- Promote new psychosocial and biomedical intervention trials that focus on the moderators and predictors (e.g., biological, genetic, behavioral, experiential, environmental) of intervention response

and side effects in different patient populations. This will be done throughout the disease course, and throughout the clinical research and drug development pipelines.

Follow exploratory trials with prospective trials to determine if using predictors enhances recovery.

Use research on the biological causes of disorder to inform and develop psychosocial and biomedical interventions that target core features of disease, assess outcomes appropriate to the course of illness under study, and develop study designs that have impact on these features.

Develop new technologies (e.g., software for enhancing or building cognitive skills, small molecules for molecular targets to develop medications) that can advance the development of new interventions.

Design more innovative and comprehensive intervention studies by building on existing data from administrative records, epidemiological studies, and previous clinical research. These may include clinical strategies already used by some and showing promise for improving symptoms or managing side-effects, but need research validation to either dissuade use or foster more wide-spread adoption.

Strengthen ongoing research that examines the balance between adverse effects and beneficial effects of psychosocial and biomedical interventions in order to enhance the understanding of cost/benefit ratios of specific treatments and support additional research that examines how to minimize or better manage side effects. Achieve a balance between efficacy and safety within a unified study, rather than addressing them in isolation in separate studies.

Accelerate research that maximizes the ability of current treatments to reduce symptoms, improve adherence and functioning, and minimize side-effects. Ensure that this research also accounts for cultural/ethnic diversity.

Strategy 3.2: Expand and deepen the focus to personalize intervention research.

Adopting novel approaches in clinical research is essential to investigating new, brain-behavior-environmental targets for intervention research in conjunction with a broader focus on an individual's functioning as a whole. When developing interventions, we will:

Broaden the focus of what is meant by outcome measures in treatment research to include assessments of daily functioning, presence of side effects, and adherence to treatment and other indicators of recovery. Expand the time course for studying intervention effects to examine longer-term alterations in outcome/disorder trajectory.

Broaden the focus of what is meant by outcome measures in prevention research by focusing on targets relevant to particular phases of the trajectory of illness, including neurobiological and behavioral measures. In cases where interventions are being used to preempt disorder, the targets could be improvements in neurobiological or behavioral functioning, rather than reduction in symptoms.

Develop standard measures of functional outcome for psychosocial and biomedical intervention research across a range of disorders and diverse populations (age, sex, ethnicity/race, educational backgrounds). Children have traditionally been an under-served population for the development of new interventions with functional outcomes.

Adopt a comprehensive health care perspective by designing studies that take into account illnesses that co-occur with mental disorders (e.g., heart disease, substance abuse); or that address the effects of taking multiple prescribed medications (e.g., conditions that may increase the risks involved in using a particular medication).

Ensure that study designs encompass a more comprehensive assessment of treatment side effects that includes impact on functioning and patient preferences.

Expand research on treatment adherence to include systematic assessments on why patients do not adhere to treatment regimens, as well as how patients self-manage or individually tailor their treatments.

Develop psychosocial and environmental interventions to improve adherence.

Strategy 3.3: Strengthen the application of mental health

interventions in diverse care settings by examining community and intervention delivery approaches and how they may affect intervention outcomes.

Mental health interventions are delivered by a wide variety of providers in different settings. For example, preventive interventions may be implemented in schools, in the workplace, or by communities at large. Treatment interventions can be delivered, for instance, by primary care doctors, social workers, clinical psychologists, or psychiatrists. In order for intervention development research to succeed, it must incorporate the perspectives of these various providers and take into account the diverse systems in which interventions are delivered.

Incorporate the perspectives of the family, immediate community, and providers into intervention research from the initial stages of development.
Develop early interventions, taking into consideration that these may be delivered by people outside of the traditional mental health systems, such as teachers, community leaders, and pediatricians.
Determine how different settings of care (e.g., clinics, private patient care, hospital, in-home care, schools) affect intervention outcomes, as well as side effects.
Support research that tailors psychosocial and biomedical interventions to different kinds of providers (e.g., psychologists, psychiatrists, psychiatric nurses, social workers) and different intervention settings (e.g., schools, mental health clinics, community health clinics).

Strategy 3.4: Identify and systematically study elements of personalized mental health care.

Each individual at risk for or suffering from a mental illness presents a unique set of characteristics, whether they are genetic, environmental, experiential, developmental, or a combination of these factors. As previously noted, mental health interventions must adapt to the needs and circumstances of each individual they are designed to help. Therefore, an environment in which mental health care adopts a personalized approach where individual characteristics (e.g., biological, cultural, socioeconomic) are considered is expected to optimize outcomes. Similarly, patient preference is a powerful indicator of how well someone will adhere to treatment and must also be part of a personalized approach to mental health intervention.

Further develop adaptive designs for psychosocial and biomedical intervention research that include patient preference.
Identify the components of interventions that are necessary for improved outcomes and clarify what aspects can and cannot be safely modified when working with different populations (e.g., different cultural and ethnic, socioeconomic, and age groups).
Enhance participation in clinical research to better reflect the diversity and complexity of the mentally ill population through improved approaches for engaging and working with different cultural, ethnic, and socioeconomic groups, and through improved dissemination of information on existing clinical research and related recruitment efforts.
Develop tools for mental health care providers to detect and monitor mental illness progression.
Develop tools for individuals and families to monitor and gauge their own or their family member's illness (e.g., home testing kits to monitor medication levels), thereby enhancing self-management of their illness.

Sidebars: Strategic Objective 3

1. Advances in understanding fear extinction: PTSD

Recent NIMH-supported research has made significant strides in understanding the nature of anxiety-related disorders such as posttraumatic stress disorder (PTSD), leading to the potential for the

development of new, more effective interventions for those suffering with this disorder. While research has been examining the details of the brain's "fear circuitry" and how it relates to anxiety disorders for decades, more recently investigations have been focusing on the mechanisms by which the brain adapts to and extinguishes fear.[19] An exciting discovery is the recent recognition that fear extinction in the brain is an active learning process, not a passive process of forgetting.[20] Researchers have identified a specific chemical that binds to brain cell receptors (NMDA partial agonist d-cycloserine) which may help to improve extinction learning.[21] This line of research has moved from using models in the laboratory to successful tests in people with a fear of heights.[22] Additional studies are now underway to examine how this knowledge can be used to help those suffering from anxiety disorders such as PTSD. This research provides hope that our new understanding of the neuronal and cellular mechanisms of fear extinction can be applied to the development of new pharmacologic and behavioral therapies to promote more rapid recovery among those suffering with this disorder.

2. Advances in the personalization of mental health interventions

NIMH continues to support novel research that seeks to understand how interventions developed to alleviate the burden of mental illnesses can be tailored to ensure the best treatment for a specific individual. While effective treatments are available, there is considerable individual variation in treatment response depending on a range of biological and psychosocial factors. From the perspective of treatment, we know that all mental disorders are highly variable across people (e.g., not everyone displays depression in exactly the same way). We are just learning how to predict which treatment will be best for any given individual.

Recent research has shown specific genetic variations to be linked to non-response and to suicidal thinking that sometimes occurs among people taking the most commonly prescribed class of antidepressants (selective serotonin reuptake inhibitors, or SSRIs).[23] , [24] These newly identified gene variations may prove useful in identifying patients who need closer monitoring, alternative treatments and/or specialty care when being treated with SSRIs.

Going forward, NIMH clinical research will not only assess overall group differences, but also individual patterns of intervention response. The goal is a personalized approach to treatment. Ultimately, we hope that patients and their clinicians will decide on the best treatment based on clinical presentation, personal and family history, and a range of biomarkers including genetic variation and brain imaging results that will predict the optimal medical or psychosocial intervention. By shifting our research towards detecting individual predictors of response, NIMH hopes to provide clinicians with the information they need to choose the best available treatment for each patient.

Strategic Objective 4: Strengthen the Public Health Impact of NIMH-Supported Research.

Through research, evaluation, and collaboration, we will further develop the capacity of the Institute to help close the gap between the development of new, research-tested interventions and their widespread use by those most in need.

NIMH's mission depends inherently on our ability to understand the nature and developmental course of these disorders, enabling the development of research-based interventions for treatment and prevention. The Institute's role, however, does not end there. To pave the way toward prevention, recovery, and cure, we must find ways to ensure that the interventions and information we generate can be used by patients, families, health care providers, and the wider community involved in mental health care.

Our sister agency, SAMHSA, supports the delivery of services to build resilience and facilitate recovery in communities across the United States. NIMH supports research, not services. However, an important part of our mission is to support research that will optimize services. For instance, NIMH research identifies factors that may enhance access to mental health services, improves the quality of and lowers the cost of care, and strengthens the means by which new interventions are broadly disseminated and

implemented. NIMH also pursues numerous dissemination efforts. Since our founding, NIMH has consistently sought the most effective and efficient methods to communicate our findings to the research community, the providers of mental health services, and the public at large.

Yet, how will we know if we are succeeding? Are the products of our research reaching those most in need of it? Are we providing the right information at the right time to the right people? To answer these crucial questions, we must closely monitor our research portfolio and our dissemination activities, and evaluate them in the context of impacting public health.

Finally, to achieve our public health mission, we must rely on our alliances with those who are also concerned with the prevention, recovery, and cure of mental illnesses. By building new or strengthening already existing partnerships with our many stakeholders—whether they are patients, families, service providers, advocacy groups, our sister agencies in the Public Health Service, or others—we can better understand the needs, questions, and concerns of those intended to benefit from the research we support. Working together more closely and efficiently will help to advance the science of mental health and lead to a quicker realization of our common goals. NIMH planning with regard to this objective is more fully described in the 2006 report of the NAMHC's Workgroup on Services and Clinical Epidemiology Research entitled "The Road Ahead: Research Partnerships to Transform Services."

To strengthen the public health impact of NIMH-supported research, the Institute will:

Strategy 4.1: Improve understanding of the factors that affect access to service, quality and cost of services, and the means by which newly discovered effective mental health interventions are disseminated and implemented.

To ensure that our research findings are translated into clinical practice, we must examine the context in which they will be delivered, and provide a knowledge base that better enables patients, their care takers and health providers to adopt proven strategies to promote mental health and treat mental disorders. To do so, NIMH will:

- Stimulate research that develops and tests novel models and methods on ways to best implement mental health interventions to diverse groups and populations (e.g., age, sex, stage of illness, racial/ethnic groups, rural, urban).
- Support research that identifies barriers and limitations to the uptake and implementation of interventions by various stakeholders (e.g., payers, patients, service providers) and subsequently use this knowledge to develop more effective models for implementation.
- Expand research efforts to identify factors that will improve access to service as well as better the quality and lower the costs of services.
- Include stakeholder input in the development of services research.
- Nurture partnerships with other NIH institutes and other Federal agencies regarding services research.

Strategy 4.2: Improve the research and dissemination activities of the Institute through monitoring and evaluation.

Through improved research monitoring and evaluation efforts, we will be better positioned to ensure that supported research is aligned with the Institute's scientific priorities. Also, as new research findings unfold and communication mediums continue to change, the Institute's dissemination strategies will need to be regularly evaluated and adjusted to ensure that our stakeholders are receiving the information they want and need. To do so, NIMH plans to:

- Monitor NIMH's research portfolio to ensure that supported work continues to match closely with the Institute's stated research priorities.
- Evaluate the impact of NIMH's existing research programs and dissemination strategies via an

ongoing process of evaluation and identify opportunities for improving them.
Support the development of indicators and metrics, including usability and satisfaction tools, to monitor the impact of dissemination efforts for various stakeholders.
Experiment with and evaluate new technologies for information dissemination (e.g., pod-casting, e-books) and make better use of existing media.
Assess the type of information that different stakeholders want and their preferred modalities of communication (i.e., know the audiences) and incorporate this into future dissemination efforts.

Strategy 4.3: Strengthen partnerships between NIMH and its stakeholder groups.

The success of the Institute's mission depends on the effective collaboration of all stakeholders in the field of mental health. This requires strengthening our current partnerships and working to build new ones so that we can understand the needs, capabilities, and limitations of the field as we work together to move forward.

Strengthen partnerships between NIMH and its stakeholder groups (e.g. payers, service providers, patients, families, advocacy groups, professional organizations).
- Improve dialogue to provide a clearer understanding of stakeholders' needs, as well as NIMH's role and what we have to offer.
- Establish new relationships with systems of care that have common interests (e.g., Departments of Education, the criminal justice system).
- Emphasize the scientific basis of mental health research findings in the information and resources provided to stakeholders.
- Strengthen the partnership between mental health care providers and researchers.

Strategy 4.4: Strengthen NIMH's relationships with other Federal agencies that address mental health issues.

Advance participation in the activities of the Federal Action Agenda (the SAMHSA-led Federal response to the President's New Freedom Commission report) by contributing research findings to address the priorities set forth in the agenda.
Strengthen our collaboration with the Centers for Medicare and Medicaid Services, the Centers for Disease Control and Prevention, the Department of Veterans Affairs, and the Food and Drug Administration to inform our clinical research.
Continue to work closely with other NIH Institutes with related missions.
- Build further scientific collaborations around areas with high co-occurrence of mental disorders with other disorders, such as heart disease and diabetes.
- Continue to capitalize on opportunities provided by cross-NIH initiatives, such as the NIH Roadmap for Medical Research and the NIH Blueprint for Neuroscience Research.

Sidebars: Strategic Objective 4

1. Cost effectiveness of intervening

The cost of mental illness is staggering, with estimates of $100 billion each year for the direct costs of care and significantly more for indirect costs, including $193 billion alone for lost earnings among individuals with serious mental illnesses.[25] , [26] NIMH continues to support a number of studies that demonstrate to policymakers, employers, health providers, and other decision-makers the tremendous cost savings that arise from investing in effective interventions for these disorders. For example, research has found that workplace depression screening, outreach, and enhanced treatment improves employees' health and productivity, leading to lower costs overall to the employer.[27]

The cost savings of interventions may be demonstrated at all stages in life, including childhood. Targeted preventive interventions that help reduce conduct problems in children are cost-effective when compared to the personal and societal costs of delinquency and crime that can arise from untreated childhood conduct disorders. By demonstrating the long-term benefits of implementing evidence-based mental health interventions, NIMH research can provide compelling evidence of ways to improve the personal and economic components of mental health care.

2. Providing a knowledge base to move evidence-based interventions into practice.

Despite their proven ability to alleviate mental illness, many tested interventions take far too long to be adopted into common practice, with some never reaching those most in need of them. Numerous barriers exist to prevent the successful integration of evidence-based interventions within clinical and community practice. Improving the fit between effective interventions and the care settings in which they are delivered is an important focus of NIMH services research. NIMH researchers, for example, are exploring new strategies to advance the dissemination and implementation of efficacious interventions in individual practices, on the community level, and even the state level. One such project involves working with the state of California to test the effectiveness of a theory-driven model to promote the adoption, implementation, and sustainability of an evidence-based intervention for children in foster care into county-wide systems.

In addition, NIMH researchers are seeking new methods for delivering evidence-based interventions to hard-to-reach populations, often making use of innovative technologies. For example, a recent study demonstrated that an Internet-based, self-managed cognitive behavioral therapy can help reduce symptoms of PTSD and depression.[28]

Finally, to ensure that evidence-based interventions have maximal benefit to public mental health, NIMH researchers are studying the best approaches for adapting proven interventions to the needs of diverse populations. For example, Critical Time Intervention (CTI), an intervention to prevent homelessness among persons with mental illness when they move from one living situation to another, has proven to be both effective[29] and cost-effective[30] for men moving from the shelter to the community. It has also been shown to be effective for formerly homeless veterans returning to their communities after psychiatric hospitalization.[31] A current study is seeking to adapt CTI for men and women moving from incarceration to the community. Taken together, this body of knowledge will maximize the impact that scientific discoveries can have in the service of public health.

Appendix A

Development Process for the NIMH Strategic Plan

This Strategic Plan was developed using a multi-stage process that solicited input from NIMH's staff and stakeholders. The first stage involved developing the Institute's Vision and Mission Statements, as well as the Institute's overarching scientific objectives. These objectives, developed with assistance of the NAMHC, are broad goals that capture the diversity of topics the Institute must focus on in order to achieve its mission. The seven scientific objectives, successively building in scale from the most basic neuroscience and behavioral science to the broad societal dissemination of mental health research and treatment best practices, are to:

1. Understand the neuronal and behavioral basis of mental disorders and how they deviate from normal processes.
2. Develop reliable, valid diagnostic tests and biomarkers for mental disorders.
3. Define the genetic and environmental risk architecture of mental disorders.
4. Develop interventions to prevent occurrence and/or reduce relapse of mental disorders.
5. Develop more effective treatments that have minimal side effects, reduce symptoms, and improve daily living.

6. Conduct clinical trials that will provide practitioners with treatment options to deliver more effective personalized care across diverse populations and settings.
7. Create improved pathways for dissemination of science to mental health care and service efforts.

The second stage in the Strategic Plan's development involved identifying the current state of the science for each of the seven scientific objectives, as well as gaps and opportunities for research advancement. This was accomplished through a series of Institute-wide brainstorming sessions, the results of which identified the four objectives that serve as the basis for this Strategic Plan.

Once an initial draft of the Plan was complete, it was posted on NIMH's website and public feedback was encouraged (see Appendix B). The draft Plan was also presented to the NAMHC in order to solicit council members' comments. The draft Strategic Plan was then edited based upon the received feedback, its text and layout were finalized, and the finished draft was publicly released.

Appendix B

Public Comment on the NIMH Strategic Plan

A draft version of the NIMH Strategic Plan was made available to the public, via the NIMH website and postal mail, between November 20, 2007, and December 21, 2007. In total, the Institute received emails and letters from more than 550 individuals, groups, and organizations regarding a broad range of mental health-related topics. We would like to thank everyone who took the time to provide feedback on the draft Strategic Plan. Numerous edits were made to the Plan during its finalization process based on the comments that were received. Public comments were also forwarded to the Institute's research divisions so that NIMH staff members could be made further aware of the public's concerns and suggestions.

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Previous Reports

Breaking Ground, Breaking Through: The Strategic Plan for Mood Disorders Research, July 2002. Summarizes the current state of the science on major depression and bipolar disorder across the life span, as well as recommendations of research priorities to achieve scientific goals.

Pathways to Health: Charting the Science of Brain, Mind, and Behavior (PDF file, 75 pages), 2002. The first research strategic plan developed to help the NIMH set priorities and future directions for research on mental disorders and mental health.

NIMH Five-Year Strategic Plan for Reducing Health Disparities (PDF file, 33 pages), November 2001. This 5-Year strategic plan for reducing health disparities prioritizes ongoing research, research training/capacity building and public information outreach and dissemination activities.

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NIMH FY 2011 Funding Strategy

NIMH Fiscal Year 2011 Funding Strategy for Research Grants

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