DOCUMENT RESUME

ED 453 924 PS 029 487

TITLE	From Cells to Selves: Biobehavioral Development.
INSTITUTION	National Inst. of Child Health and Human Development (NIH), Bethesda, MD.
PUB DATE	2001-02-00
NOTE	28p.
AVAILABLE FROM	NICHD Clearinghouse, P.O. Box 3006, Rockville, MD 20847; Tel: 800-370-2943 (Toll Free); Fax: 301-496-7101; Web site: http://www.nichd.nih.gov/publications.
PUB TYPE	Opinion Papers (120) -- Reports - Descriptive (141)
EDRS PRICE	MF01/PC02 Plus Postage.
DESCRIPTORS	Adolescent Development; Aggression; Behavior Disorders; *Brain; *Child Development; Child Health; Chronic Illness; Developmental Disabilities; *Disabilities; Federal Government; Intervention; Learning Processes; Long Range Planning; Mental Retardation; Mission Statements; Neuropsychology; Prosocial Behavior; *Research Methodology; *Research Needs; Social Development; Socialization; *Strategic Planning; Violence
IDENTIFIERS	Brain Development; Continuity; Discontinuity; Fetal Development; National Institute Child Health Human Development; Risk Taking Behavior

ABSTRACT

Key to the mission of the National Institute of Child Health and Human Development (NICHD) is answering fundamental questions about how a single fertilized cell eventually develops into a fully functional adult human being and how a multitude of genetic and environmental factors influence that process. This document details part of NICHD's strategic plan for achieving its mission, focusing on goals and objectives to guide NICHD research on biobehavioral development over the next 5 years. The document first describes NICHD's mission and outlines the strategic planning process. The introduction then presents basic concepts underlying the NICHD biobehavioral strategic plan. The first section of the document discusses 2 scientific goals of the strategic plan. The first concerns biobehavioral bases of developmental continuities and discontinuities from birth through parenthood, and includes biobehavioral influences of social behavior and socialization, influence of sex/gender throughout development, fetal behavior, understanding and facilitating learning in typically developing populations, and adolescence. The second concerns the development of individuals with disabilities and chronic diseases, including therapeutic interventions for developmental disabilities and related conditions, developmental neurobiology underlying the emergence of prosocial versus violent and aggressive social behaviors, and biobehavioral effects of the interaction between the individual, technology, and multimedia sensory experiences throughout development. The second section of the document examines research technologies and resources deemed relevant, including data collection and analysis related to neural networks and dynamic systems for analysis of development, animal models, functional neuroimaging, and brain tissue banks. The document concludes by identifying the need for predoctoral and postdoctoral training programs that integrate experiences across the many disciplines relevant to biobehavioral research and the need to create new opportunities for effective and productive multidisciplinary research endeavors. Appended is the roster of members of the strategic plan working group providing advice on the development of this document. (KB)

FROM CELLS TO SELVES

Biobehavioral Development

National Institute of Child Health and Human Development

FROM CELLS TO SELVES

Biobehavioral Development

National Institute of Child Health and Human Development

Contents

The NICHD Mission

The National Institute of Child Health and Human Development (NICHD) seeks to ensure that every individual is born healthy, is born wanted, and has the opportunity to fulfill his or her potential for a productive life unhampered by disease or disability. The Institute further strives to help parents have the children they want, at the times they want them, and to ensure that every mother experiences a pregnancy free of adverse complications. Key to the success of this mission is answering the fundamental questions of how a single fertilized cell eventually develops into a fully functional adult human being and how a multitude of genetic and environmental factors influence that process for good or ill.

Programs at the NICHD are based on the concepts that adult health and well-being are determined in large part by episodes early in life, sometimes before birth; that human development is continuous throughout life; and that optimal outcomes of development are important not only to the individual but to society. NICHD research is also directed toward restoring or maximizing individual potential and functional capacity when disease, injury, or a chronic disorder intervenes in the developmental process. Thus, the NICHD mission truly spans the life cycle, and much of the health and well-being of our population depends on the success of the Institute's research.

The Strategic Planning Process

During 1998 and 1999, the NICHD staff engaged the scientific community in jointly developing a strategic plan to facilitate achieving its mission. The initial framework document for this plan, *From Cells to Selves*, highlighted four areas for immediate strategic development and described a series of scientific goals under each area. These four areas were as follows:

- *Genetics and Fetal Antecedents of Disease Susceptibility* includes the interaction of the genotype with socioeconomic, environmental, and psychological factors in the fetal and postnatal environment that contribute to health or the pathophysiology of diseases.
- *Reproductive Health for the 21st Century* comprises the biological and behavioral factors that allow couples to have healthy children when they want them and the reproduction-related conditions that may affect women during and after their reproductive years.
- *Developmental Biology: Understanding Normal and Abnormal Development* consists of the basic biological science necessary to understand early development *in utero* and through the time when many organ systems form.
- *Biobehavioral Development* includes research to better understand the developmental processes involved in forming cognitive, learning, emotional, social, and physical behaviors, and the biological and environmental factors that make infants, children, and adolescents more susceptible to behavioral disorders or to adopting risk-taking and violent behaviors.

This document refines the goals and objectives outlined under the area titled "Biobehavioral Development."

To help establish the more detailed research agenda that follows, the NICHD convened a working group comprising distinguished scientists (see Appendix) from around the country and asked them to collaborate with Institute staff to identify and prioritize research goals and to suggest appropriate strategies to meet those goals. The working group drew upon ongoing planning efforts, previous emphasis areas, recent forums, workshops, conferences, and research findings to develop a draft of the strategic plan that would guide the Institute's research agenda in biobehavioral development for the next 5 years.

The draft plan was posted on the NICHD Web site to allow members of advocacy groups, nonprofit organizations, the scientific community, and the general public to comment. In addition, the Institute shared the plan with members of the National Advisory Child Health and Human Development Council and with the Friends of the NICHD, a coalition of more than 100 professional and patient organizations committed to the Institute's scientific mission. After consolidating and reviewing all comments, the NICHD revised and finalized the plan. This document is intended as a targeted, but flexible, blueprint that can be modified as new scientific findings, research opportunities, or resources become available.

Introduction

If we truly wish to understand human health and behavior and to devise effective, practical ways to apply basic science advances to improving human health and behavior, we must first understand the complex interplay among external, biological, and behavioral factors that results in a human being. In addition these interactions, and all related functions, processes, and outcomes, must be understood in the context of developmental changes that occur over time. Without understanding fundamental biological factors such as brain structure and function, changing hormone effects, or genetic contributions, it will be difficult to develop more effective ways to treat, let alone prevent, complex developmental conditions such as mental retardation, autism, attention deficit disorder, and learning disabilities. Nor will we be able to truly understand how one learns to read or communicate or how to best teach and parent our children. By simultaneously addressing developmental problems and the impact of external factors on biological and behavioral functioning, scientists could use research funds more effectively, while saving critical time and guarding the fragile hopes of affected individuals and their families.

Certain basic concepts underlie the NICHD biobehavioral strategic plan:

- The nervous system represents a continuum of neural processes involving the entire brain, cranial nerves, the autonomic nervous system, and the peripheral nervous system.
- Behavior is an emergent property of the nervous system, driven by environment, context, and experience and requiring specific neurophysiological states and processes.
  - ➢ By "behavior" we mean both internal and external actions or responses originating from factors such as cognition, language, learning, memory, academic skill acquisition, emotion, cognitive-based social interactions, and planned motor function.
  - ➢ By "environment" we mean external factors such as nutrition, health care, environmental toxins, schooling, and the full range of experiences of children in the family, community, and broader society.
- The biobehavioral interface is inherently bi-directional.
  - ➢ Biobehavioral development research targets the development of behavioral processes (along with their interrelations with molecular, genetic, cellular, and neural systems), whole organ processes, and environmental factors to understand how these interrelations contribute to typical and atypical development. A full understanding of the impact of these interrelationships requires a more integrated research approach. Studies that focus on only one level of analysis are not sufficient.
- Traditional disciplinary boundaries must be crossed. For example, scientists or teams of scientists who have an understanding of both neural processes and social behavior must be recruited to study social development.
- The creation and use of animal models must be supported and expanded. Cross-species comparisons are no longer sufficient. Conceptually sophisticated studies must take into account phylogeny and ontogeny.
- Researchers will be encouraged to include examining long-term behavioral consequences in studies incorporating biological manipulations (e.g., gene

manipulation, reproductive intervention, or hormonal manipulations).

- There also is a strong need to examine the behavioral consequences associated with decisions about important biological events throughout the lifespan, for example, the decision to breastfeed or the decision to take hormone replacement therapy.

By targeting the biobehavioral approaches outlined in this strategic area, the NICHD plans to expand its leadership role in addressing significant developmental health problems ranging from chromosome abnormalities associated with cognitive deficits to childhood violence. In addition, the Institute's effort can unravel the scientific mysteries of how children learn, think, plan, feel emotions, decide, and act in ways that not only support their well-being but also contribute to society. This is no small effort; it requires targeting existing knowledge gaps, integrating multidisciplinary approaches, and encouraging collaborations to translate basic science into practical solutions. In terms of knowledge gaps, amazingly little scientific information exists to tell us exactly which aspects of behavioral experience are essential to human development, or how experience and behavior relate to the biological functioning of the developing organism. Therefore, the main goals of the following strategic research areas are to expand our knowledge of (1) how the developmental processes associated with behavior and experience are incorporated into biological structures and mechanisms, (2) how biological processes shape behavioral development, and (3) how this new scientific information can be used to devise relevant and effective interventions to improve the lives of children.

These goals require an unprecedented integration of several scientific disciplines involving behavioral, social, and basic biological sciences. In turn, this multidisciplinary, integrative approach promises to greatly stimulate interest and subsequent scientific advances in human behavioral development, as well as in complex child health and development issues.

Scientific Goals of the Strategic Plan

The following strategic areas were identified on the basis of the most recent breakthroughs in developmental research. They represent areas where gaps in our current understanding of development exist, as well as where the integration of biological with behavioral science can best be applied to the developmental problems faced by children in our society today.

Biobehavioral Bases of Developmental Continuities and Discontinuities: From Birth Through Parenthood

The NICHD believes that it is important to emphasize development when conducting biobehavioral research. It is critical to apply biobehavioral research paradigms to questions that are relevant to specific developmental periods, developmental transitions across periods, or commonly experienced developmental episodes. Scientists need to learn much more about the biobehavioral bases of development and the continuities and discontinuities that occur as children mature from birth until they themselves reach parenthood. The behaviors of interest include cognition, perception, attention, memory, speech, language, emotional and social developmental behaviors, and the ability to regulate behaviors (e.g., behavioral inhibition, sleep regulation, and feeding).

The processes are also bi-directional. Biobehavioral studies should be able to address not only how behavioral/environmental processes influence biological development but also how biological factors influence behavioral/environmental interactions. It is as important to investigate the impact of culture and early environments on biology as it is to understand the biological correlates of behavioral development. For example, significant differences in health and developmental outcomes between and among racial and ethnic groups are most likely the result of complex interactions between basic biological processes and environmental factors such as poverty, education, and cultural realities. (For an expanded discussion of NICHD strategic planning for research addressing racial and ethnic health and developmental disparities, see the NICHD strategic plan titled "Health Disparities: Bridging the Gap.") Many of the emphasis areas described below target critical knowledge gaps.

Biobehavioral influences of social behavior and socialization throughout development

Societal and biomedical researchers often focus their attention on negative issues, such as illness, stress, or violence. As a result, research concerning processes associated with positive social behavior, wellness, and health has been neglected. To better understand the body's ability to cope with the challenges of daily life or even serious disease, it is essential to identify active processes underlying good health and states of psychological and physical well-being.

The benefits of positive experiences, socialization, and social support are no longer controversial. It has long been known that primate newborns, including humans, require social interactions for normal development. When these social interactions are lacking during development because of social deprivation or inappropriate social experiences, the result may be physical and emotional illness, including asocial behaviors. Likewise, more recent human epidemiology studies have revealed that social isolation, even in adulthood, increases the risk of morbidity or mortality from all causes. For example, cardiovascular disease, the leading cause of death in both men and women, is more prevalent in individuals who live alone. Thus, it is important to understand the mechanisms and processes underlying both the positive and negative effects of social interactions. Shared neural substrates (e.g., hypothalamic pituitary adrenal (HPA) axis substrate, which affects both social behavioral responses and physiological functioning) are responsible for both positive social behavior and optimal physiological functions, such as cardiovascular or immune function. This knowledge suggests mechanisms through which positive social experiences mediate both physical and mental health. Unfortunately, limited funding and the fact that this topic crosses traditional scientific disciplines have slowed the development of research in this important area.

Given this understanding, studies that are grounded in only one level of analysis are no longer sufficient. For example, social behavior, like other behavioral states, is the result of physiological events, which emerge from specific biological processes and states of the nervous system. However, research on social behavior and social development traditionally has focused on behavior-behavior relationships rather than on physiological-behavioral interactions.

The physiological approaches to social behavior and the nature of the process of socialization are relatively recent and uncommon. Biobehavioral studies that do exist in this field tend to use physiological parameters (including psychophysiological measurements, brain imaging, etc.) as secondary or correlative variables. Although interesting, this approach is limited and can address neither the neural mechanisms mediating social behavior nor the mechanisms through which social behavior affects physiology. Within an integrative model, researchers assume that social context and experience can impact physiology and, conversely, that physiology can limit or optimize social behavior.

For example, social behaviors in primates, including humans, are regulated not only by the central nervous system (CNS) but also by several cranial nerves necessary for social engagement (i.e., looking, listening, and vocalizing). The brain regions, including cortical areas, that control the neural pathways necessary for social engagement have direct connections with brainstem areas regulating cardiovascular, pulmonary, and immune function. Greater knowledge of this integrated system is essential to improve our understanding of the mechanisms and health consequences of social behavior and the processes involved in socialization. Understanding the functional organization of the nervous system offers insight into mechanisms through which positive social behaviors control health, growth, and restoration.

Social behavior varies across species, and knowledge of this natural variation has advanced our understanding of processes responsible for social behavior. In addition, changes induced through specific manipulations of the nervous system have provided an increased awareness of the neurobiology of this system.

We now know that neuroendocrine and autonomic processes regulate positive social experiences in a variety of animal models. For example, neuropeptide hormones, produced primarily in evolutionarily ancient areas of the brainstem but acting throughout the brain, are implicated in both positive social behaviors and the systems responsible for good health. An awareness of the novel properties of neuropeptide hormones and their mechanisms of action provides a unique perspective on the physiological basis of positive social experiences and suggests mechanisms through which positive experiences and social support improve welfare and protect us from the stress of life.

It is essential to understand these processes in the context of the lifespan. For example, socialization is a lifelong process of learning to function within social groups. Harmonious and constructive functioning improves quality of life and contributes to a stable, productive society. Conversely, inadequate socialization can undermine the family, degrade all levels of society, and, if not controlled or rectified, negatively influence the organizations and institutions that society builds.

In terms of specific research directions, the following questions have been targeted as requiring emphasis during the next decade:

- How do biobehavioral processes underlie socialization, taking into account growth and maturation as well as social contact, mother-infant dyadic interactions, caregiver-child interactions, teacher-student interactions, gender-based interactions, friendships, and adversarial encounters, among others?
- How can the healthful bonding of mother to child and child to mother be enhanced so that the child is well prepared for subsequent attachments?
- How can we encourage a healthy development of the human brain's structure and function so that it serves healthy, effective social adaptation throughout life?
- How can competent communication skills best be cultivated?
- What factors help determine the effectiveness of each individual child as a social agent, a person, and a citizen?
- How do children learn to be happy, to have fun, and to benefit from play, given both its attendant pleasures and acrimonies?
- How can children be helped to develop the personal and social strengths necessary for becoming effective adults in a highly mobile and technical society with its unstable social networks?

- Modern technological advancement, including increased reliance on electronic communication, has not taken neural systems into account. Therefore, a range of questions should be answered. For example, what are the biobehavioral and health consequences of the increased amount of time spent by both adults and children in social isolation because of interaction with this technology?

Influences of sex/gender throughout the developmental process

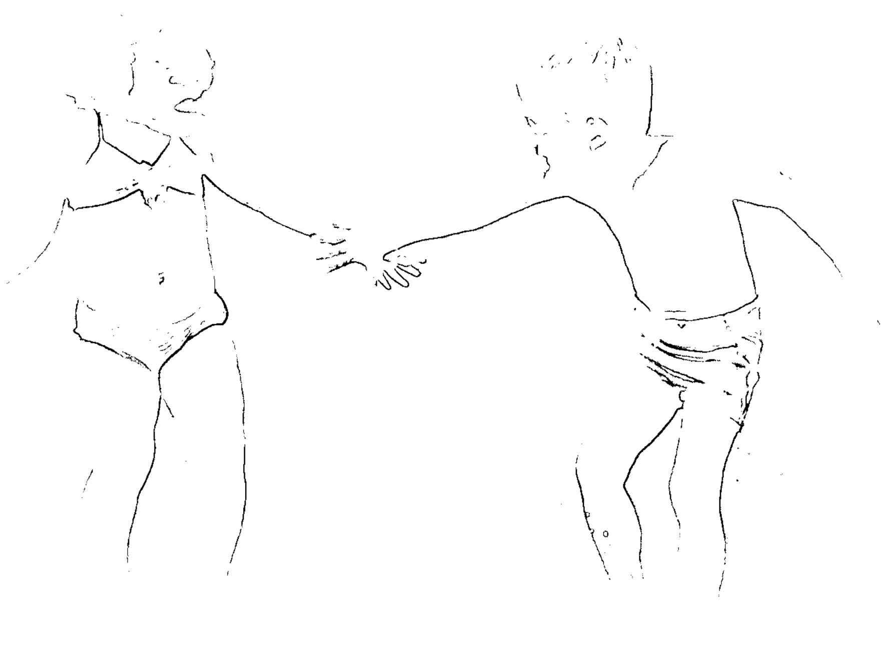
A large number of descriptive studies have documented sex/gender differences; however, few studies examine why behavioral and related disease differences exist between males and females. Therefore, researchers must go beyond these descriptive studies to understand the developmental processes that produce these differences and the consequences on health throughout the lifespan and on individual and social behavior.

To better understand the influence of sex/gender differences in optimal biobehavioral development across the lifespan, priority should be given to multidisciplinary research that (1) simultaneously examines biological and behavioral development and cultural influences and (2) examines how these mechanisms lead to differential outcomes between the sexes. The level of adoption of gender role and how this is tied to development of the self also should be researched further.

Areas to be targeted and questions to be answered in the next decade include the following:

- The physiological and genetic differences between males and females *in utero* and postnatally predispose males to be more susceptible to a variety of difficulties and specific disorders. What is the role of biological gender, coupled with social factors tied to gender role norms, in affecting a child's risk for disease or developmental disability?

- How do biological gender and gender roles influence differences in the ability to adapt to and cope with stress, variations in cognitive performance and emotional development, and willingness to engage in risk-taking behaviors?



- How do the interactions of gender role, culture, and biological factors affect biobehavioral outcomes in different cultures?

Fetal behavior

We know little about what fetal and early postnatal behaviors, and their interactions with biological and environmental factors, tell us about the developing fetus or neonate, or how such behavior is related to physical and neurological status and perinatal outcome. Studying the fetus will contribute new theories concerning the process of behavioral development. Specifically, prenatal research can help identify transformational or ontogenetic factors that specify how behavioral capacities change from one stage to the next.

With the exception of information concerning the development of sensory systems during pregnancy, we know little about fetal behavioral abilities over the total course of fetal development in any mammalian species. Even in rodent species that have been studied in late gestation and early postnatal life, little is known concerning earlier behavioral antecedents of learning, memory, and perceptual abilities. This is a crucial lack of knowledge with respect to the coming age of genome manipulation research and presents major concerns regarding the safety of gene manipulation, as well as the related field of assisted reproduction technology (embryo splitting, sperm injection, living animal cell cloning.) Studying the behavioral effects of genome and reproduction manipulations depends initially on detailed descriptions of the fetal developmental behavioral phenotype. Where scientifically possible and justified, assessing the development of relevant behavioral phenotypes should be a part of all fetal studies manipulating genes and reproductive methods.

We also know very little about relationships between fetal behavior patterns and abilities, competencies, and development later in life. It is clear that most, if not all, postnatal behavioral abilities depend initially on nervous system growth and physiological development during the embryonic and fetal periods. However, scientists do not know how the rate of this early development correlates to postnatal developmental abilities. For example, is rapid fetal development predictive of later competence? Does retarded development *in utero* mean that postnatal development will also be retarded? Are relatively high versus low fetal hormone levels related in any important ways to development during infancy and behavior in adolescence? Is fetal immune system development related to postnatal immune competency, disease risks, or behavioral effects at later life stages, including old age? Such questions cannot be answered unless we know if, when, and how fetal processes are related to postnatal growth, physiology, and behavior. This means that fetal biobehavioral phenotypes need to be related to phenotypes and outcomes in later developmental stages. Studies that follow measurement of fetal phenotypes into postnatal life will advance our current knowledge and are critical for assessing the safety and validity of applications of animal model findings to humans.

During the past 20 years we have learned a great deal about how maternal behavior and environment can affect fetal development. Drugs, alcohol, smoking, viral infection, other teratogenic substances from the home and work environment, and some types of malnutrition are detrimental to normal fetal development, especially brain growth, and are risk factors for abnormal postnatal development. We need a better understanding of the influence of maternal endocrine status on fetal outcomes and long-term developmental consequences, including the influences of maternal thyroid, oxytocin, and vasopressin. A large, but contradictory, body of literature suggests that psychosocial and other environmental stressors on the pregnant mother can have detrimental effects on the pregnancy outcome and offspring development. On the other hand, there is almost no information concerning conditions that may enhance fetal development and maximize postnatal abilities, or that minimize the effects of risk factors experienced during pregnancy. With the exception of late pregnancy studies, and terminal studies with no prenatal or postnatal end points, there are almost no studies relating acute effects of fetal environment events to prenatal or postnatal developmental processes or outcomes. This is especially true in the area of maternal stress research in both animals and humans. Animal models documenting the existence of acute effects mediated through the mother on the fetus are critical for understanding which events can affect fetal development and for justifying longitudinal developmental outcome studies of environmental events, such as maternal stress.

Biobehavioral studies of the fetus will help to identify novel approaches to promote the health and development of preterm infants and other at-risk infants. These approaches will not necessarily emerge from simple attempts to mimic either the fetal or full-term newborn environments, but from appreciation of the interplay of factors that drive behavioral development. In some respects, the preterm infant is a fetus that is challenged to survive and develop in an age-atypical environment. Understanding the capacities of the fetus *in utero* may help to identify new approaches for the clinician to promote the development of the preterm infant.

It is important to understand the details of fetal behavior, not merely general measures of fetal reactivity such as gross motor activity or changes in heart rate. Characterization of behavioral organization will require new technologies for accessing the fetus, as well as more sophisticated quantitative methods for measuring temporal, sequential, and spatial patterns. In addition to activity and the state of the nervous system per se, fetal behavior can be influenced by other factors internal to the fetus (physiology, morphology), features of the sensory environment (mechanical and chemical stimuli), and environmental context (physical constraint, gravitational loading, uterine activity, etc.) As the fetus develops into a competent organism in its own right, fetal researchers must apply more inclusive models of behavioral control in studies of prenatal behavioral and neural development. Study of learning in the neonate has progressed from using artificial stimuli and contingencies to using stimuli that are ecologically relevant during early development. For example, most studies of prenatal habituation have employed artificial stimuli, such as the vibroacoustic stimulation produced by an artificial larynx. If learning has adaptive significance during the perinatal period, one may expect that using stimuli that are important to the fetus or newborn would better assess learning capacities.

Understanding and facilitating learning in typically developing populations

Researchers need to better understand the conditions underlying optimal acquisition of higher cognitive skills such as language, reading, math, reasoning, and critical thinking. Research in this area requires a truly integrated, biobehavioral approach. Such research also must relate our understanding of neuroanatomical development, developing brain processes, and neurochemical and neuroendocrine effects with learning behaviors and environmental influences (e.g., curriculum, mode of presentation of content, home environment influences, peer influences.) Researchers must pay particular attention to disparities in learning outcomes as functions of biological and environmental factors.

For example, there is a need to understand the patterns of neural organization that lead to skilled reading and skilled mathematics. Identifying the environmental factors, such as specific instructional approaches, that lead to these patterns in typical learners can demonstrate what interventions lead to these patterns in children with learning disabilities. In addition, researchers must understand how patterns of neural organization in typical learners relate to long-term outcomes in academic skills, vocational skills, and life satisfaction.

Researchers must also gain a better understanding of the relationships among neuroanatomical substrates, higher cognitive skills, and social learning in the developing organism. Furthermore, scientists need to identify the neural mechanisms and cognitive pathways mediating social behaviors and social learning. Researchers already have identified possible neural substrates underlying social behaviors and attachments, including the hippocampus, cerebellum, prefrontal lobe, and pathways involving the temporal lobe. For example, slower reaction times on vigilance tasks (presumably mediated by prefrontal lobe inhibition and executive function) are associated with poorer social and nonverbal understanding. Early frontal lobe damage has been associated with poor empathetic and social development. Early cerebellar damage predicts poor social competence and nonverbal functioning as well as poor comprehension of language sequences during social communication. The next step requires greater mechanistic understanding of these types of associations to advance our knowledge of cognitive and social development.

The following questions target additional gaps in knowledge concerning learning in typically developing populations:

- How does earlier acquisition of skills affect later neural development and higher cognitive skills?

- What are the possible biological interventions for facilitating higher cognitive learning?

- What are the relationships between early motor development, neural plasticity, and later higher cognitive skill?

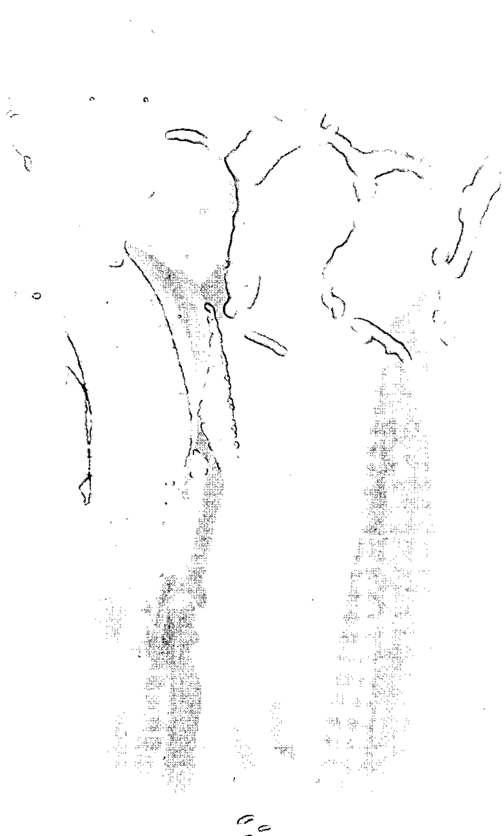
- What is the relationship between the quantity and quality of computer/electronic media use and neurophysiological, cognitive, language, and social development?

Adolescence

There has been little comprehensive research on adolescence, despite the many important neurobiological, hormonal, and social behavior interactions to be addressed during transitions into, from, and throughout this developmental period. Researchers need a better understanding of both typical adolescent development and adolescent development in atypical populations. Such research should examine the factors leading to increased vulnerability during adolescence, in terms of emotional, behavioral, conduct, and social development difficulties, and the subsequent effects of these difficulties on adulthood.

To successfully negotiate the developmental transition between youth and adulthood, adolescents must maneuver this often stressful period while acquiring skills necessary for independence. Because certain behavioral

features, including age-related increases in risk-taking/novelty-seeking behaviors, are common among adolescents of diverse mammalian species, animal studies may aid in understanding this process in adolescent humans. For example, pubertal increases in gonadal hormones are a hallmark of adolescence, although there is little evidence for a simple association of these hormones with the behavioral changes observed during adolescence. Likewise, prominent developmental transformations are seen in prefrontal cortex and limbic brain regions of adolescents across a variety of species, alterations that include an apparent shift in the balance between mesocortical and mesolimbic dopamine systems. Developmental changes in these stressor-sensitive regions likely contribute to neurobiological and behavioral interactions that lead to the unique socioemotional and behavioral characteristics of adolescence. Understanding this process and its outcomes is a major topic area for adolescence researchers.



Developmental psychologists are concerned about the lack of research on adolescence, especially about the transitions into and out of adolescence. Therefore, researchers need to establish baseline data regarding typical adolescent biobehavioral development. For example, hormonal changes associated with puberty occur much earlier in development than the actual onset of puberty. The developmental course of these changes is highly variable, making the onset of preadolescence difficult to predict. Furthermore, the onset of hormonal change varies according to ethnic background, with some females 6 to 7 years of age showing signs of preadolescence. This is a downward shift of 5 to 10 years for females in some cases and suggests the importance of studying endocrine stages, independent of age, as the predetermining factor of precocious adolescence.

Significant structural neuronal growth changes occur during adolescence that affect behavioral development. Some evidence suggests that there is a right hemisphere growth spurt and pruning between ages 13 and approximately 16 years. Associated with this growth spurt and pruning is the development of the ability to abstract multidimensionally. Frontal and parietal areas of the brain are the last to myelinate, which continues up through age 15 or 16 years. Because it is not clear how behavior and environment interact with these structural changes, investigating the behavioral associations of structural brain changes during adolescence and their interactions with genetic and environmental factors is a priority for NICHD biobehavioral research.

Neural pathways associated with specific cognitive functions may differ during adolescence when compared with adulthood or childhood. For example, adults appear to rely on a left hemispheric prefrontal region of activation associated with a task of inhibition, whereas adolescents rely on right hemispheric opercular frontal cortex and caudate for comparable levels of performance on the same task. Such research suggests the possibility of adolescence as a "sensitive" or "critical" period for some types of neurobiological processes and, by association, specific types of social and cognitive learning. Researchers must gain a better understanding of these adolescent neurofunctional sensitivities and the role they play during the adolescent period. Particular types of learning or other experiences may be critical for certain types of cognitive and/or socioemotional outcomes during specific times during adolescence.

Adolescence also appears to be a time of increased vulnerability to emotional disturbance or stress. Animal models have shown that stress in the form of threat and attack during adolescence can alter the balance between vasopressin and dopamine in the brain, resulting in inappropriate aggressive behavior in early adulthood. Although there has been much emphasis on behavioral and social antecedents and outcomes of emotional disturbance or stress during adolescence, the underlying biological interactions are poorly understood. This is also an important area of research for adolescent study.

The following questions target key areas of adolescence research:

- What are the links between the biological processes responsible for puberty and the behavioral changes associated with these processes?
- What factors help optimize adolescent biobehavioral outcomes?
- How do individuals with developmental disabilities, learning disabilities, or chronic diseases transition through adolescence?
- What are the biobehavioral antecedents and consequences of variations in typical and atypical pubertal development?
- What are the neurobiological antecedents of, and influences on, the emergence of expertise and skilled behavior during adolescence?
- How do adolescent outcomes relate to long-term biobehavioral development?

Development of Individuals With Disabilities and Chronic Diseases

There is a lack of research examining the interactive factors associated with processes of biological, neurocognitive, and behavioral development specific to, and characteristic of, individuals with mental retardation and other developmental disabilities or chronic diseases over time. There is a significant gap in knowledge concerning how children with disabilities or chronic childhood diseases fare socially, cognitively, vocationally, and adaptively during adulthood. In addition, research is needed to increase understanding of the continuing developmental needs of adults with developmental disabilities or with chronic diseases that start in childhood. Such research is particularly important for predicting the developmental course and risk/protective factors associated with a particular disability or chronic disease as well as for developing effective, developmentally sensitive interventions across the lifespan.

Although there is a great deal of information on the biological, neurocognitive, and behavioral processes that cause disabilities, there is little information concerning how these factors interact to produce disabilities. The biobehavioral research agenda gives priority to projects that specifically target these interactions, while recognizing the need to continue advancing our knowledge of the basic mechanisms that underlie conditions that precede disabilities.

Priority should be given to studies of risk factors for children who are generally at high risk for neurodevelopmental disorders due to multiple adversities, particularly children in poverty either in the inner city or rural areas. The total burden or interactive burden of multiple risk factors in such children may result in very different trajectories of development than in children who have only one risk factor. Better social policy and interventions might result from knowledge gained regarding multiple adversities and interaction effects.

Therapeutic interventions for developmental disabilities and related conditions (including mental retardation and other atypical development)

This emphasis area focuses on exploiting and disseminating basic scientific advances to further develop innovative therapies (including new pharmaceuticals) as well as to refine and enhance the use of interventions for specific developmental problems. Studies are needed to clarify the mechanisms and processes concerning a specific disease or disability and the efficacy of related therapeutics, including pharmacological, educational, and psychological mechanisms and interventions. Researchers also must examine why some interventions are effective for one individual and not for another.

Such efficacy assessments should include measures relevant to independent and adaptive functioning. Additional long-term followup studies are needed to gain a better understanding of the impact and outcomes associated with specific interventions over time. Both animal models and human applications are pertinent.

There has been little research addressing the efficacy, long-term side effects, and outcomes of a wide range of commonly used pharmacological agents in children. Such research requires both cross-sectional and longitudinal approaches. This emphasis area is particularly relevant for children with multiple disorders, dual-diagnosis disabilities, or mental retardation. It is also relevant for guiding practitioners to use more effective pharmacological interventions for children with developmental disabilities.

The long-term effect of medications on the developing brain is an under-investigated area. Long-term developmental outcomes for prenatal and/or postnatal exposure to medications (in particular, prolonged use of antibiotics) also need to be addressed. Anatomical, biochemical, and neurobehavioral effects in animals could be examined to study the effects of antibiotics. Studies of neuroimmunologic involvement in autism or other disabilities, or chronic childhood diseases, and how these parameters change with different pharmacological or nutritional interventions are important.

Furthermore, there is a need for well-designed elimination/challenge studies of nutritional interventions for children with developmental disability. For example, we do not know if there are dietary implications for individuals with certain disabilities (e.g., autism and Fragile X syndrome).

A pressing need exists to develop effective interventions for children with developmental disabilities involving learning deficits or behavior deficits (e.g., stereotyped, aggressive, self-injurious behaviors) that interfere with optimal development. This intervention research would include developing both new pharmaceuticals and other biological or behavioral strategies based on emerging scientific advances. This research will require identifying and clarifying the neurobiological, behavioral, and environmental mechanisms and processes underlying efficacy. Therapeutic research also must address the optimal timing of interventions throughout development. In addition, a great need exists to develop innovative interventions that address deficits in reading, mathematics, written communication skills, language usage, communication strategies, and learning ability or retention. The development of intervention strategies and devices should be emphasized for both typical and atypical developmental populations.

There is also a need for research into developmental plasticity. This type of research holds promise for increasing our understanding of experience-dependent influences on brain organization in children with developmental disabilities and learning disorders, as well as for typically developing children.

Although many advances have been made in techniques for facilitating the acquisition of language and educational skills in atypically developing individuals, with the exception of occupational training, little attention has been given to the actual use of these skills in everyday life. Similarly, advances in both behavior therapy and nonsedative drugs have brought abnormal behaviors under control in many people and show even more promise for the future. Children with Down Syndrome or Fragile X syndrome may be taught to read and to use language abilities in social interactions in clinical settings, but little is known about the generalization of these treatments, skills, and behaviors to everyday life. Such questions can best be answered by observational studies in daily life settings. Therefore, behavioral therapy and skills training research for the disabled should routinely include a component that assesses and documents the use of these skills or presumed behavior controls during the individual's everyday activities. This information will be useful in assessing the utility of the methods for clinical applications and in assessing the cost-benefit relationships for enhancing quality of life.

Health behavior and risk factors in childhood

Although information about health behaviors in adulthood (e.g., smoking, diet, exercise) and their effects has grown dramatically in the past decade, researchers need to learn much more about health-related behaviors during childhood and how they influence developmental as well as lifelong health outcomes. The biobehavioral approach to this type of research will examine not only the biological disease or injury processes themselves but also the behavioral and external factors preceding, maintaining, aggravating, or interacting with these processes. Identification of biobehavioral risk factors in childhood, which predispose the child to injury, illness, eating disorders, obesity, chronic disease, and unplanned pregnancy, are a priority. Biobehavioral intervention studies, including developmental, behavioral pharmacological studies, are needed to evaluate the biological systems affected by the intervention being studied. It is also important to include variables that will help capture differences that occur across population groups and to extend these studies to community-based applications.

Human epidemiology and rodent behavior studies suggest that deviant development in grandparental generations caused by nutritional and chemical insults, and even environmental or psychological stressors, can be passed on to grandchildren by nongenetic processes. For example, low birth weight of the grandmother caused by environmental conditions is correlated with lowered birth weight in grandchildren. Using certain hormones during pregnancy to protect against premature delivery can result in increased cancer risk in grandchildren. Such nongenetic transmissions of detrimental effects across generations has barely been considered, let alone studied, as causes of human health and behavior problems. It seems likely that many human problems associated with lower socioeconomic status may result from such nongenetic cross-generation effects. Well-designed retrospective human studies may be useful in more firmly establishing this concept. Experimental studies are possible only in animal models. Such studies would be especially important with respect to establishing the validity and potential scope of nongenetic intergenerational effects. (For an expanded discussion of NICHD strategic planning for research addressing disease susceptibility, see the NICHD strategic plan titled "Genetics and Fetal Antecedents of Disease Susceptibility.") In light of an expected explosion of genetic studies as genome functions become identified, the possibilities of nongenetic intergenerational factors could easily become lost in gene enthusiasm.

Developmental neurobiology underlying the emergence of prosocial behaviors versus violent and aggressive social behaviors

Several lines of animal-model and human evidence indicate the important role that genes, hormones, neurotransmitters, neuroendocrine factors, neurocircuitry, and neuroreceptors play in the development of complex social behaviors, including the formation of social affiliations, parental care, asocial behaviors, and social aggression. Much more needs to be learned, however, about how these biological factors, interacting with brain development, cognition, and environmental and situational influences, result in prosocial, empathetic behaviors or, alternatively, in social avoidance, social aggression, and violent behaviors, particularly over time.

Emotion is normally regulated in the human brain by a complex circuit consisting of the orbital frontal cortex, amygdala, anterior cingulate cortex, and several other interconnected regions. There are both genetic and environmental contributions to the structure and function of this circuitry. Impulsive aggression and violence most likely arise as a consequence of faulty regulation of negative emotions. Research on the neural circuitry of emotion regulation suggests new avenues of intervention for at-risk populations. Understanding how environmental, biological, and developmental factors modulate aggressive responses to environmental and situational stimuli in humans will aid our ability to predict and prevent human violence, while facilitating our ability to construct effective interventions for promoting prosocial behaviors and preventing human aggression and violence. Biological factors underlying these issues are difficult to elucidate and have not been well studied. They deserve additional emphasis and study.

Interactions between individual biological processes and environment affecting or facilitating development

Clarifying and better understanding the interplay among genetic and environmental influences on neurobehavioral development in populations with typical development, learning disabilities, developmental disabilities, or other developmental disorders is another major research target. To pursue this research, investigators must develop efficient and inexpensive age-appropriate instruments to help understand and explain genetic variations and gene/environmental effects on behavioral variability across populations.

Perhaps most importantly, given the tremendous progress in identifying the human genome, we now need to decipher the behavioral correlates of various gene expressions. Since the reciprocal relationship between gene expression and behavior requires a multidisciplinary approach to understanding, gene manipulation studies should involve collaborations between molecular biologists and behavioral developmental researchers.

The emergence of practical methods for producing identical twins for animal research studies enables a new dimension of controlled experimental developmental behavior genetics. Embryo splitting can be used to produce four to eight identical individuals from a single blastocyst in animal models, ranging from mice to nonhuman primates. With these techniques in animal models, identical twin mothers can carry identical twin fetuses through pregnancy and, if needed, through early postnatal development. One or more twins can be assigned to experimental treatments; others can serve as controls. These techniques will be especially useful for gene manipulation, teratology, stress, and environment studies because they can unequivocally separate genetic from environmental factors in experimental research. Well-designed studies using these techniques in basic developmental research, as well as targeted studies of developmental abnormalities, will provide information that is unavailable or difficult to interpret using traditional developmental designs, including human identical twin studies.

Significant gaps exist in researchers' understanding of the characteristics of the developmental course of the brain/endocrine systems, making this an important area to study. In addition, because the endocrine system plays an important role in stimulating neurobiological activity, it is important to gain a better understanding of the interaction of neuroendocrine and environmental factors on typical and atypical development and behavior. This interaction is particularly important as a response to internal and external stressors.

Prenatal and perinatal exposure to infectious agents and toxins has been linked to pathogenesis of developmental disabilities and neuropsychiatric disorders. Researchers need to learn more about the possible connections and identify the mechanisms by which such outcomes can occur, how such effects can be treated, and any related long-term outcomes.

Both human and animal research during the past 20 years has shown that behavior and environment can have important consequences for immune processes. Recently, it has been shown that disease and immune processes can also affect behavior. Thus, it appears that emotional and cognitive processes can affect immune functioning and that immune processes can affect neural activity. Some rodent and primate studies suggest that environmental and physical stressors experienced during pregnancy can affect the postnatal development of immune processes. This raises the question of relationships between immune system development during prenatal and postnatal life stages, medical health and disease resistance, and health and disease-related behaviors. Theory, but little data, has suggested that fetal brain development, including laterality and hormone effects, and lifetime disease risk may be associated with fetal immune system development. Immune system effects are also certain to be a major concern in the application of gene manipulations to disease-related and behavior-related human problems. Therefore, studies relating immune system development to neural, hormonal, and behavioral processes are important targets for new biobehavioral knowledge.

Biobehavioral effects of the interaction between the individual, technology, and multimedia sensory experiences throughout development

Researchers know very little about the impact of computers and other technologies on the development of children—including physiological, neural, social, and emotional development, both positive and negative. Computers and other new technologies also hold the promise of useful, individualized, and specific interventions for children with developmental and learning disabilities.

Neuroplasticity in development, learning, and memory

It is critical to understand the interactive effects of behavior, environment, and neuronal cell motility as part of the developmental process. This research needs to include investigating the factors that control axonal growth and targeting as well as understanding how learning and experience influence neuronal "pruning."

Hormones and stimulants (such as caffeine) have pronounced effects on dendritic spine shape and motility, potentially affecting the efficiency of associative learning networks. Research is needed to increase understanding of how these events occur and influence outcomes throughout development. In addition, recent studies demonstrate that neurons within the temporal lobe may be regenerated, opening several important avenues of research on human learning and development.

Research Technologies and Resources

The following technical development areas are relevant for all the biobehavioral research areas targeted in the previous section, and are highlighted because of their importance for studies specifically addressing developmental issues.

Data Collection and Analysis Related to Neural Networks and Dynamic Systems for Analysis of Development

Investigations in the emphasis areas should incorporate innovative methods of statistical or mathematical analysis to increase understanding of developmental trajectories, developmental growth curves, dynamic systems for representing multiple influences, and developmental transitions. In addition, these improved analytic techniques are necessary for understanding the complexity of neurobehavioral actions or responses. Investigators also require tools to represent "fluid behaviors," such as skilled performance, or the change in this "fluidity" with maturation in a skilled motor performance. Modeling approaches should be emphasized to provide a means of studying how systems emerge and change, a key to understanding development. These should include neural network modeling, dynamical systems theory, and CMU-style or other computational models. At present, statistical models deal only with stationary targets. Computational approaches to learning and change, and the promise of developmental simulations as a new tool, are important technologies to be further developed in developmental biobehavioral science.

A great need also exists to develop new statistical techniques that will permit the analyses of multiple variables in situations where there may be relatively few subjects. For example, current statistical techniques that insist on 10 to 1 ratios between subjects and variables do not apply to the data produced by more advanced imaging techniques, such as fMRI, PET, and multichannel ERP and EEG studies involving 64 or more electrodes.

To achieve maximum efficiency of effort and expenditure, large databases should be made accessible to a wider range of researchers. Since large grants collect massive amounts of data and often analyze only a fraction of it, the remaining data could be valuable to other investigators, or could be combined with other data sets to make the data more useful. Data pooling could be accomplished through a network of linked databases in lieu of one centralized database. Standardizing data coding would help with managing the rapidly increasing volume of information that already exists and is expected to continue into the future. With improved data accessibility and coding, it may be possible to analyze questions that were not feasible before on an individual basis. However, to accomplish this, issues of intellectual property rights need to be addressed because of the potential for problems resulting from collaborative efforts.

Animal Models

Some of the most fundamental, mechanistic aspects of biobehavioral research will have to be examined in animal models. Emphasis should be placed on developing parallel behavioral models in animals (including the mouse and monkey) as well as in humans. In addition, it is critical to develop and use animal models of particular syndromes associated with developmental disabilities to investigate biobehavioral influences on development, from conception through young adulthood.

Although invertebrate, insect, and rodent models of developmental processes are crucial for identifying and understanding basic biobehavioral mechanisms and processes, they may have limited utility in assessing the scope of effects and safety of current and future genetic and nongenetic (assisted reproduction) advances. Study of animal species with genomes, reproductive biology, growth, and physiology closer to that of humans will be necessary to assess many of these technical and knowledge advances before they can safely be used on humans. Past experience has shown that human tragedies may result from failure to first adequately test science applications on appropriate animal models. Recognition of this problem and education of persons at all levels of the application process is especially important in the current context of animal rights. Without adequate support from the NIH, the Federal Government, and the general public, these crucial studies of the most appropriate models of human processes may become difficult, if not impossible, to pursue.

Functional Neuroimaging

The ability to use new functional neuroimaging modalities (e.g., EEG, ERP, fMRI, DTI, MEG, MRS) to link physical parameters in the brain with specific behaviors, and to do so over the course of development, presents investigators with an unprecedented opportunity. These tools allow earlier diagnosis and enable researchers to examine the effects of interventions. The use of such techniques will be important for addressing questions relevant to many of the strategic emphasis areas in biobehavioral development discussed in the previous section. However, it is impossible to conduct functional neuroimaging studies without specifying functional tasks to be studied. Functional genomic and functional imaging research require accurate analyses of the phenotype and the development of age-specific activation tasks likely to target specific brain areas involved in emotional and cognitive functioning. Therefore, this research agenda also emphasizes the development of age-specific model tasks.

It is also important to take advantage of the use of multiple techniques on the same subject, for example, co-registration of subjects involved in both fMRI and ERP procedures. One technique yields more information about spatial resolution (fMRI), whereas the other yields good temporal information (ERP). When combined, data from both techniques will tell a more interesting story and provide complementary information to enhance research insights.

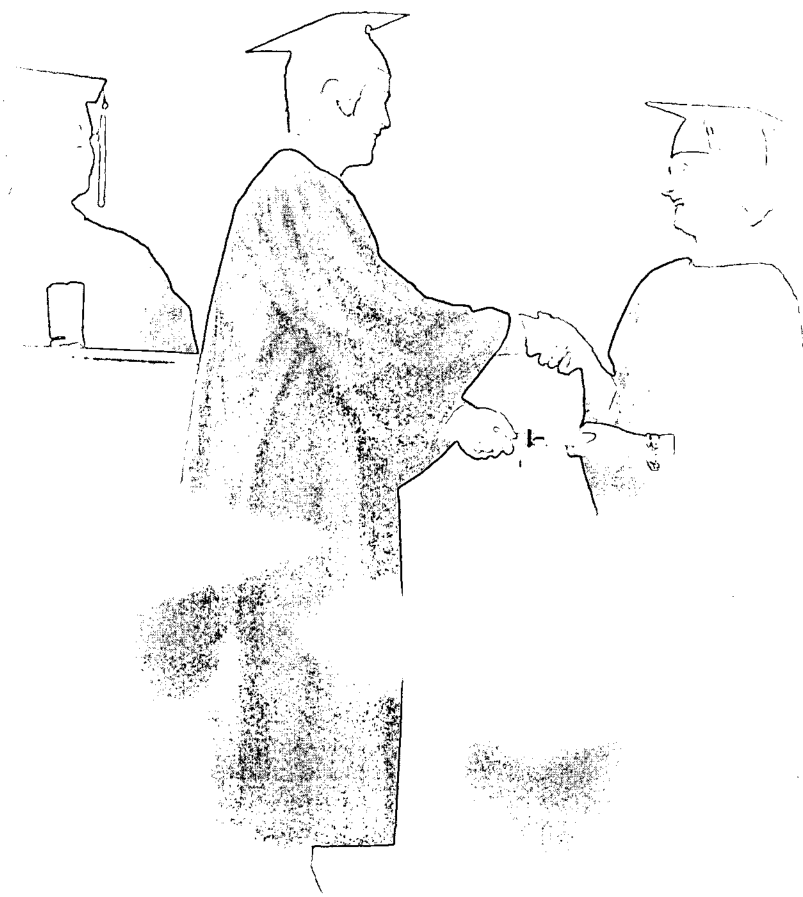
Brain Tissue Banks

Although the Human Genome Project may reveal which proteins (e.g., transcription factors, enzymes, receptors) are implicated in various developmental disorders, the individual biochemical states of cells in different regions of the brain can be determined only with tissue from autopsies. Recruiting families to donate tissue at the death of individuals with such conditions (e.g., with autism, fragile X syndrome, or Down syndrome) is an important undertaking. Behavioral profiling of individuals whose brains have been donated is necessary, and sharing brain tissue among researchers is important in standardizing brain sectioning or brain preservation among investigators. Given these needs, it is essential to create a network of brain tissue banks and to improve the way that investigators communicate the results of neuropathological examination targeting different syndromes.

Training and Education

A tremendous need exists for predoctoral and postgraduate training programs that integrate experiences across the many disciplines relevant to biobehavioral development research, in general, and to the strategic emphasis areas listed above, in particular.

It also is imperative to integrate advanced training in the behavioral and basic biological sciences to enhance and create new opportunities for effective and productive multidisciplinary research endeavors.



Appendix—Roster of Advisors

Although this document has benefited from the input of many scientists within and outside the NICHD, and from the general public, we wish to particularly note the advice of the following members of the strategic plan working group:

Duane Rumbaugh, Ph.D., Co-Chair
Georgia State University

Frances Horowitz, Ph.D., Co-Chair
The City University of New York

Sue Carter, Ph.D.
University of Maryland, College Park

Donald Cohen, M.D.
Yale University Medical Center

Dennis Molfese, Ph.D.
University of Louisville School of Education

Gene Sackett, Ph.D.
University of Washington

Sally E. Shaywitz, M.D.
Yale University School of Medicine

Howard Silver, Ph.D
Consortium of Social Science Associations

William P. Smotherman, Ph.D.
Binghamton University
State University of New York

For additionol copies of this strategic plan, or for more information on contacts or related issues, please contact the NICHD Clearinghouse at

P.O. Box 3006
Rockville, MD 20847
Phone: (800) 370-2943
Fax: (301) 496-7101
Web: http://www.nichd.nih.gov/publications/

For additional information about other NICHD strategic plans and research, please visit our Web site at http://www.nichd.nih.gov/

U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health
National Institute of Child Health
and Human Development

ary 2001

NOTICE

Reproduction Basis

☐ This document is covered by a signed "Reproduction Release (Blanket)" form (on file within the ERIC system), encompassing all or classes of documents from its source organization and, therefore, does not require a "Specific Document" Release form.

☒ This document is Federally-funded, or carries its own permission to reproduce, or is otherwise in the public domain and, therefore, may be reproduced by ERIC without a signed Reproduction Release form (either "Specific Document" or "Blanket").

EFF-089 (3/2000)