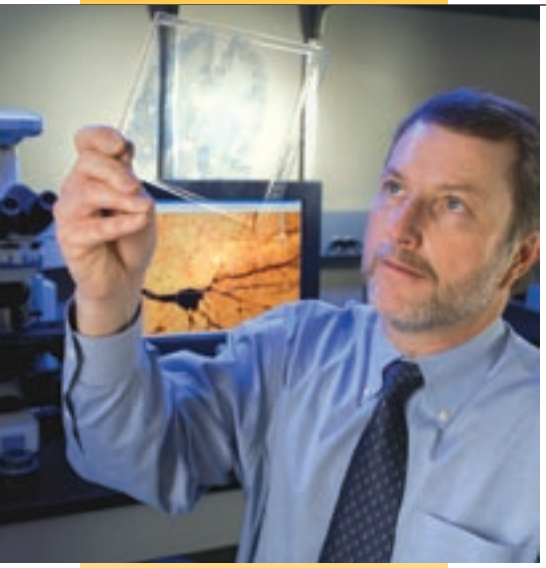
the Autism Phenome Project



Autism today

According to statistics from the Centers for Disease Control, nearly 1 in 166 children born today have, or will eventually have, autism. That means that an estimated 1.5 million American families struggle with a neurodevelopmental disorder that can limit a child's lifelong potential for independence and normalcy. Autism has no cure. Its symptoms and severity differ among individuals, yet all affected by the disorder have difficulties initiating and sustaining social interactions, impaired communication skills and restricted, repetitive patterns of behavior.

One of the major roadblocks to understanding the causes of, and finding effective treatments for, autism is that it has diverse outcomes. Some individuals have seizures, but others do not. Some have troubling gastrointestinal problems, but others do not. Some have severe developmental delays, but others have normal or even enhanced IQs. This heterogeneity raises the possibility of several types of autism (autism type A, autism type B, etc.) with a variety of causes. This heterogeneity limits both scientific progress and clinicians' abilities to effectively treat the disorder. Thus far, research on autism has been too fragmentary to allow precise definitions of autism subtypes based on biomedical and behavioral characteristics.

The most comprehensive study yet

The Autism Phenome Project is the largest and most comprehensive assessment of children with autism ever undertaken. It aims to distinguish subgroups, or phenotypes, of autism based on thorough biomedical and behavioral analyses of affected children.

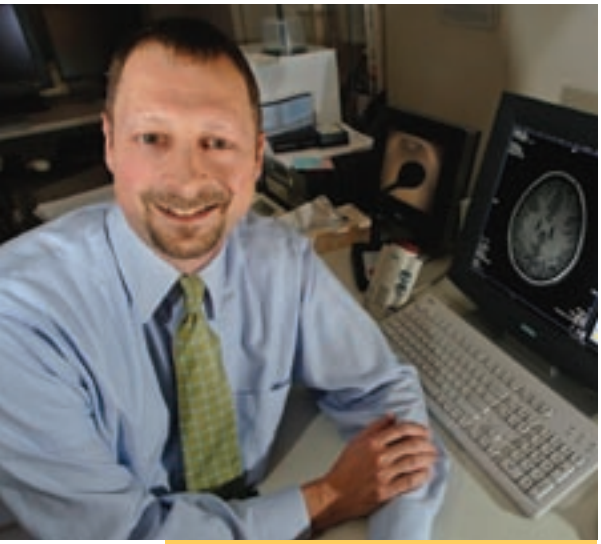
Expected outcomes

The Autism Phenome Project promises to change the way autism is defined, diagnosed and treated by gathering unprecedented kinds and amounts of biomedical and behavioral data from 1,800 children and their families over the course of five years. The outcomes will be significant:

- A database of biomedical, experiential and behavioral information that defines different types of autism (these data will be accessible to the world community of autism scientists)
- A foundation for future research into the causes of each of the various types of autism
- A rich resource for establishing genes associated with different types of autism—DNA is collected from all study participants and their families
- A resource for the development of novel prevention and treatment strategies for different types of autism

A COMPREHENSIVE PROCESS

Led by UC Davis M.I.N.D. Institute Research Director David G. Amaral and co-directed by developmental psychologist Sally Rogers, a multi-disciplinary team of scientists has begun a pilot study of 55 children and their families. The project, which had been in the design phase for two years, will ultimately include 1,800 children initially 2 to 4 years of age at multiple sites across the country and perhaps internationally. Data gathered from children of both sexes with a diagnosis of autism will be compared to children with mental retardation or developmental delay as well as to typically developing children. The Autism Phenome Project is a longitudinal study with families returning for follow-up evaluations for several years.



Families in the Autism Phenome Project participate in four visits constituting phase one of the study. Evaluations take place at the M.I.N.D. Institute and Imaging Research Center in Sacramento and at the Center for Mind and Brain in Davis.

During the first year of the project, each participating child is involved in the following analyses:

Medical evaluations. An initial examination is conducted by a pediatrician with expertise in developmental disorders. Standard data such as height, weight and head circumference are gathered, as well as blood, hair and cheek swab samples for biomedical analyses. Some samples are gathered from siblings and parents as well. Families are also asked to submit medical histories and existing medical records. Every effort is made to minimize invasive procedures, such as blood draws. A novel aspect of the medical examination is the acquisition of a three-dimensional digital image of the child's face, which is used to detect dysmorphic features that are often indicative of genetic or metabolic disorders.

Environmental exposures/ Epidemiology. Current evidence suggests that more than genes determine whether or not a child will have some forms of autism. Some children may be more susceptible to environmental toxins. Parents are therefore asked questions related to their child's exposures to environmental toxins and household products, along with their dietary habits. Samples are examined for exposure to environmental toxins such as mercury and PCBs. House-hold samples are taken to investigate possible unknown environmental exposures.

Behavior. These assessments consist of established autism diagnostic interviews, tests, parental questionnaires and observational schedules. Other tests examine specialized abilities such as imitation. Sensory processing and emotional reactivity are also evaluated.

Genomics. This part of the study utilizes the latest in genetic profiling—the microarray—to assess which genes are turned on and at what levels in the blood of children with autism. Genetic analyses also involve evaluating several genes and chromosomal abnormalities that have been implicated in the disorder.

Brain structure and function. Each child receives a structural MRI (magnetic resonance imaging) analysis of his or her brain. This determines whether there has been abnormal growth of some brain regions. Other techniques investigate the pattern of connections between different parts of the brain. Sensory processing at an elemental level is evaluated using electroencephalography.

Immune function. Abnormal immune system function has been implicated in the development and progression of certain forms of autism. Autism Phenome Project researchers use blood samples to determine whether abnormal antibodies are present. Immune system chemicals indicative of inflammation are also evaluated as well as the number and kinds of immune cells.

Proteomics and metabolomics. This part of the project consists of an exhaustive search for measurable, biological markers for the subtypes of autism. Proteomics is used to determine whether certain proteins are differentially expressed in the subtypes of autism.

Bioinformatics. This portion of the project provides support for the researchers, especially in organizing and analyzing the vast amounts of genetic and protein characterization data. Sophisticated cluster analysis strategies are used to detect patterns of study features that can be used to define subtypes of autism.

RESEARCH TEAMS

Fifty-two M.I.N.D. Institute scientists from eight research areas take part in the Autism Phenome Project. The following research team leaders manage specific aspects of the project:

Medical evaluations

Robin Hansen is the director of clinical programs at the M.I.N.D. Institute and a professor and chief of developmental-behavioral pediatrics at the UC Davis School of Medicine. Hansen is a developmental-behavioral pediatrician and researcher with vast experience in treating children with neurodevelopmental problems such as autism, learning disorders and attention deficits.

Environmental exposures

Irva Hertz-Picciotto is a professor of public health sciences at the UC Davis School of Medicine. Hertz-Picciotto researches the health effects of a variety of environmental chemicals, including lead, arsenic, pesticides and PCBs. She is president of the International Society for Environmental Epidemiology and chaired the Institute of Medicine/National Academy of Sciences 2002 Committee to Review Health Effects in Vietnam Veterans of Exposure to Herbicides. She is also principal investigator of the CHARGE (Childhood Autism Risk from Genetics and the Environment) study, which investigates environmental causes of autism and is the main entry route for participants enrolling in the Autism Phenome Project.

Behavior

Sally Rogers and Sally Ozonoff. Rogers is a professor of psychiatry and behavioral sciences at the UC Davis School of Medicine. She specializes in research on autism and other developmental disorders and treating patients with developmental disabilities, especially young children with autism and their families. Ozonoff is a professor of psychiatry and behavioral sciences at the UC Davis School of Medicine. Her research focuses on very young children with autism. She is studying the onset of autism in a prospective investigation that follows high-risk infants from birth through age 3.

Genomics

Jeff Gregg and Frank Sharp. Gregg is an associate professor of pathology at the UC Davis School of Medicine and director of the M.I.N.D. Institute's genomics facility. He is an expert in microarray technology, which he uses to perform expression studies in order to identify genes associated with autism. Sharp is a professor of neurology at the UC Davis School of Medicine. His laboratory focuses on molecular neurobiology, genomics, neural cell injury and cell death and the blood genomics of neurological disease. Before joining the institute, he led the team that provided the first convincing evidence that blood genomics could detect pathological events in the animal and human brain.

Brain structure and function

David G. Amaral and Tony J. Simon. Amaral is the Beneto Foundation Professor and research director at the M.I.N.D. Institute. He is also a professor of psychiatry and behavioral sciences. His research involves determining the neuroanatomical, behavioral and electrophysiological organization and functions of brain systems involved in memory, emotion and social behavior. He also conducts research on neurobiological correlates of autism. Simon is an associate professor of psychiatry and behavioral sciences at the UC Davis School of Medicine. As a pediatric cognitive neuroscientist, his research focuses on the neural bases of cognitive impairments seen in genetic disorders that produce mental retardation, developmental disability and psychopathology.

CHILDREN & FAMILIES

The Autism Phenome Project will owe its success to the children and the motivated family members who participate. This requires fostering close relationships among children, families and project coordinators. In addition to comprehensive medical evaluations, families are provided reports about research findings, ongoing clinical advice and gift certificates in appreciation for their participation.

Immune function

Judy Van de Water and Paul Ashwood. Van de Water is a professor of rheumatology, allergy and clinical immunology at the UC Davis School of Medicine. Her primary interests include autoimmunity, immunopathology, and molecular and cell biology. Her research emphasis is the immunobiology of autism, including food sensitivity. Ashwood is an assistant professor of medical microbiology and immunology at the UC Davis School of Medicine. His current work is directed at characterizing the role of the immune system in autism. His original research in his native England involved identification of a new variant of inflammatory bowel disease found in some cases of autism.

Proteomics and metabolomics

Howard Schulman is vice president of biomarker discovery sciences at PPD Biomarkers. Prior to joining industry, Schulman was professor and chairman of neurobiology at Stanford University School of Medicine. He is recognized for his discovery and subsequent analysis of one of the key protein kinases responsible for transmitting information from calcium-linked neurotransmitters and neuropeptides in learning and memory.

Bioinformatics

David Rocke is co-director of the Institute for Data Analysis and Visualization, a professor of applied science and a professor of biostatistics at the UC Davis School of Medicine. He specializes in the analysis of large datasets such as those generated by gene microarray experiments.

FUNDING

Funding for the initial $1.5 million pilot study was provided by the M.I.N.D. Institute. Additional funding from the National Institutes of Health, other public entities, private foundations and individual donors is being sought to continue and expand the project nationally and carry it through to completion.

COLLABORATIVE PARTNERS

To complete the Autism Phenome Project in five years, the M.I.N.D. Institute intends to partner with three-to-four collaborative sites. Initial discussions are under way with several universities with the infrastructure, personnel and willingness to participate. Depending on funding, additional sites, particularly international sites, will be solicited as partners.

About the UC Davis M.I.N.D. Institute

The UC Davis M.I.N.D. (Medical Investigation of Neurodevelopmental Disorders) Institute is a unique collaborative center bringing together parents, scientists, clinicians and educators for research on autism, fragile X syndrome, learning disabilities and other neurodevelopmental disorders.

For more information

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