



Testimony
Before the Appropriations Subcommittee
on Labor, Health and Human Services,
Education, and Related Agencies
United States Senate

**Autism Research at the National
Institutes of Health**

Statement of
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Good afternoon, Senator Harkin and members of the Subcommittee, I am pleased to present a brief review of the research activities and accomplishments in autism research of the National Institutes of Health (NIH), an agency of the Department of Health and Human Services (HHS). I deeply appreciate your continued support for our mission: making medical discoveries to improve health and save lives. In focusing today's hearing on autism we will be discussing an urgent, critical public health challenge affecting many families.

What Is Autism?

Autism is a developmental brain disorder, with onset by three years of age. We now believe that autism includes a large number of disorders that share deficits in social behavior, abnormal communication, and repetitive behaviors. Autism in turn is part of a broader continuum of syndromes called pervasive developmental disorders, now more commonly known as autism spectrum disorders (ASDs). ASDs range in severity, with classic autism being the most disabling, while others, such as Asperger's syndrome, produce milder symptoms. Among children at the more severe end of this spectrum, mental retardation, seizures, and self-injurious behaviors are common.

Current Centers for Disease Control and Prevention (CDC) estimates of the prevalence of ASDs are as high as 6.7 children per 1,000.¹ Prevalence refers to the number of affected individuals at a given point in time, essentially a snapshot.

¹ Centers for Disease Control and Prevention. Prevalence of Autism Spectrum Disorders - Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2002. Surveillance Summaries, February 9. MMWR 2007;56 (No. SS-1).

While prevalence estimates have increased many-fold since the early 1990s, it is unclear if there also exists an increase in incidence, which measures the number of new cases across time in the same population. It is unclear whether the rise in prevalence is due to a rise in incidence, better identification and awareness of the disorder, or both. A similar increase in prevalence has been observed in many countries outside of the U.S., and in virtually every study, boys are three to four times as likely to have ASDs compared to girls.²

What Causes Autism?

There is much that remains unknown about the causes of autism. Scientific research has demonstrated that autism is highly heritable, as measured by concordance rates in twins. If one identical twin has autism, there is a 60-91 percent chance the other will also have it. For fraternal twins, the concordance for autism drops significantly, to 0 -10 percent.³ While higher concordance in identical twins is not proof of a genetic cause, approximately 10 percent of autism cases with a family history of ASDs are associated with genetic mutations.⁴ Recently, a study of people with autism who did not have another family member also affected found approximately 10 percent associated with spontaneous genetic mutations.⁵ In addition, autism is frequent in children with several known

² Fombonne E. Epidemiology of autistic disorder and other pervasive developmental disorders. *J Clin Psychiatry*. 2005;66 Suppl 10:3-8.

³ Veenstra-VanderWeele, J, Christian, SL, Cook, EH (2004) Autism as a paradigmatic complex genetic disorder. *Annu. Rev. Genomics Hum. Genet.* 5:379-405

⁴ Barton M, Volkmar F, *J Autism Dev Disord.*, 1998, 28(4):273-8.

⁵ Sebat et al, Strong Association of De Novo Copy Number Mutations with Autism. *Science*. 2007 Mar 15; [Epub ahead of print].

genetic neurodevelopmental disorders, such as Fragile X, Rett Syndrome, or Tuberous Sclerosis Complex.

Identifying both the environmental and the genetic underpinnings of autism are critical first steps in bringing the full scientific power of modern neuroscience to bear on this complex set of disorders. We now have the genetic sequencing and neuroimaging tools that will permit a more thorough understanding of the neural substrates of autism. Indeed, what these scientific tools may tell us is that ASDs are illnesses with multiple causes and, much like hypertension or cancer, may be treated and possibly prevented through interventions on multiple fronts.

Importantly, these new scientific approaches will enable us to develop new diagnostic tests and rational therapies based on the biology of the illness that will permit us to detect and treat ASDs in much the same way as other medical conditions.

How Is Research Combating Autism?

Combating autism is a collaborative effort, involving several NIH Institutes, the CDC, and public-private partnerships with advocacy organizations. NIH has increased funding for autism nearly five-fold since 1997, to support broad research efforts across genetic, neuroscience, environmental, and treatment studies. Already, this investment is bearing important results for better understanding the brain abnormalities in autism, improved methods for early detection, and refining interventions for optimizing daily functioning. NIH continues to fuel this research momentum, most recently with Program

Announcements encouraging research on the characterization, genetics, pathophysiology, and treatment of autism and related neurodevelopmental disorders, as well as Requests for Applications to collect data and biomaterials from autistic individuals and their relatives for use in genomic, basic, translational neuroscience research, and clinical trials. Here I will note just a few of the recent developments that offer hope for families struggling with autism.

The recently established NIH National Database for Autism Research (NDAR) for the first time provides an open-access platform to facilitate sharing of raw research materials, foster collaborations and public-private partnerships, and enhance rapid dissemination of research findings into clinical practice. It is envisioned as a dynamic, federated system, with improvements and updates being added routinely to meet the most critical and valuable needs of the research community.

Early detection is important for improving outcomes. The National Institute of Child Health and Human Development (NICHD) and the National Institute on Deafness and Other Communication Disorders (NIIDCD) continue to partner with Autism Speaks to support the High Risk/Baby Sibling Research Consortium, an effort to improve early detection and diagnosis. The Consortium's primary project is to identify factors that may influence recurrence rates of ASDs and broader developmental outcomes in infant siblings of individuals with ASD. Recruitment of sibling and comparison groups is on target and database development and data analysis have begun.

Responding to the urgent need for an amplified autism effort, the National Institute of Mental Health (NIMH) created a new, integrated autism research program in its intramural laboratories in Bethesda. Several new clinical trials were launched in 2006 that provide opportunities for rapid progress in defining the biological and behavioral characteristics of different subtypes of ASDs and examining effects of innovative treatments for autism. Intramural researchers are also collaborating with M.I.N.D. (Medical Investigation of Neurodevelopmental Disorders) Institute and University of California at Davis scientists in a pilot of the first large-scale effort to provide a comprehensive biomedical and behavioral characterization of 1,500 individuals with autism spectrum disorders. The goal of this Autism Phenome Project is to identify the many subtypes of autism, providing guides for personalized approaches to treatment.

In addition to these efforts, NIH is striving to identify and understand environmental influences as potential causes of ASDs. The National Institute of Environmental Health Sciences (NIEHS), in partnership with the Environmental Protection Agency (EPA), supports research through Centers that focus on this important question. One of the centers, at the University of California at Davis, is conducting the first large population-based, epidemiologic case-control study of children with autism. In addition, the National Institute of Neurological Disorders and Stroke (NINDS) is providing support for a five-year prospective epidemiological study of a large Norwegian birth cohort of 75,000 women and their babies. The study, which we expect to include up to 500 children with ASDs, will examine the contribution of genetic and environmental factors to the

development of autism and other neurodevelopmental disorders; these factors include infection history, low birth weight, dietary and environmental exposure to methyl-mercury, and vaccination history.

Solving the mysteries of autism will require scientists from many disciplines working together on common problems. To launch a broad, multidisciplinary attack on autism, NIH recently created an ambitious, integrated program in order to maximize coordination and cohesion of NIH-sponsored efforts - the Autism Centers of Excellence (ACE), for which the first grants will soon be issued. Research projects will focus on identifying biological and environmental causes and preventive interventions for autism, as well as improved pharmacological and behavioral treatments. These Centers will be coordinated through NDAR and will represent the first integrated, national research effort for this disorder, with an estimated funding level of \$25 million per year.

How Can We Cure Autism?

While there is not a proven biological treatment for the core symptoms of autism, it is generally agreed that early identification and behavioral intervention is beneficial. Thirty years of study have shown the value of employing behavioral methods to enhance social skills, language acquisition, and nonverbal communication. Such gains may be evident in individual responses to particular behavioral techniques in the short term . in as little as a matter of months.

Yet even in studies where children have received the largest gains, outcomes are variable, with some making significant progress and others advancing quite slowly or not at all. A multi-study analysis of the effect of treatment indicates that behavioral treatments are most successful when they begin early, are intensive, and highly structured. Current NIH-funded research includes studies for toddlers that involve parents in the delivery of interventions at home, immediately after diagnosis, as opposed to waiting for community or other services to begin.

While medications are useful for some of the accessory symptoms of autism, such as self-injurious behaviors, we lack medical treatments for many of the core symptoms, such as social deficits. As we discover more about the causes and the mechanisms of autism, we expect to develop a new generation of medications to help children and adults affected with ASDs. Ultimately, our goal is prevention, based on early detection of risk, understanding environmental factors that increase or decrease symptoms, and development of effective interventions before behavioral and cognitive deficits appear.

The Future

The Combating Autism Act of 2006 (P.L. 109-416) was signed into law on December 19, 2006. Plans are underway to implement the provisions of this law, which calls for the establishment of a new Interagency Autism Coordinating Committee (IACC) to coordinate all efforts within HHS concerning autism spectrum disorders, including the development of a strategic plan that sets research funding priorities. Thus, broad collaborative partnerships involving

government, private industry, public and educational institutions, and families of those with autism will continue to fuel the vital research endeavors that will reveal the mysteries of this disabling disorder and lead to prevention and effective treatments.

Autism is a serious, disabling developmental illness that affects many families in this country. Research is our best hope for making a difference for these families. Given the complexity of the disorder, answers will not be as simple or as quick as we wish, but NIH is committed to bringing the best minds and the best tools to ensure that we get the correct answers that will lead to the best treatments. I therefore appreciate the interest of the members of this Subcommittee on autism research.

I look forward to answering your questions.