NIH Centers of Excellence

Autism Centers of Excellence

Overview

Why the Autism Centers of Excellence Were Established

Recent studies suggest that autism spectrum disorders (ASD) affect approximately 1 in 110 children in the United States. Because of the urgent need to better understand the causes of ASD and develop treatments for these serious and disabling disorders, Congress passed the Combating Autism Act of 2006. This Act emphasized the need to expand research and improve coordination among NIH Centers of Excellence focused on ASD. The new Autism Centers of Excellence (ACE) program, the funding of which began in FY 2007 and FY 2008, focuses on identifying the causes of ASD and developing new and improved treatments.

In response to the Combating Autism Act, the NIH Autism Coordinating Committee (ACC) formed the ACE program by consolidating the aims of two previous ASD research programs into a single research effort (see Table 4-6). The previous programs were the Collaborative Programs of Excellence in Autism (CPEA, established in 1997) and Studies to Advance Autism Research and Treatment (STAART, established in 2002 and completed in 2008). This report will focus mainly on the goals, activities, and accomplishments of the ACE program. The ACC itself also was formed at the request of Congress and comprises representatives from five ICs.

How the Autism Centers of Excellence Function within the NIH Framework

The Children's Health Act of 2000 established the Interagency Autism Coordinating Committee (IACC), which includes Federal agency representatives and members of the public appointed by the Secretary of HHS. At the request of Congress, the IACC developed an Autism Research Matrix. The matrix delineated goals and action items in epidemiology, the characterization of ASD, the role of the environment, neuroscience, screening, early intervention, specific treatments, and school and community interventions, to guide NIH-funded ASD research. ACE grantees are addressing the matrix goals, particularly the goals of identifying the causes of ASD and developing treatments.

The NIH ACC established the goals of the ACE program, and the NIH ICs share administrative and oversight responsibilities. The ACE program comprises centers and a network infrastructure. ACE centers foster multidisciplinary collaboration among teams of specialists at a single facility to address a particular research problem in depth. Each center conducts interdependent sub-projects. ACE networks unite researchers at many different facilities throughout the country; working as a unit, each network addresses a single research question. Because networks encompass multiple sites, they can recruit large numbers of participants with ASD, achieving optimal design for treatment trials. A program officer and grants management officer at the awarding NIH Institute administer each ACE award.

The Combating Autism Act of 2006 expanded the scope of the IACC. In accordance with the new law, the IACC develops and updates annually a strategic plan for ASD research and a summary of ASD research.
advances. The IACC also monitors and makes recommendations about Federal ASD-related activities. The priorities and progress of the ACE program will be an integral component of these annual activities.

In January 2009, the Interagency Autism Coordinating Committee released the first edition of its Strategic Plan for Autism Spectrum Disorder Research. Consistent with the Strategic Plan, the six ACE centers and five networks that comprise the ACE program have begun research on biomarkers, genetic susceptibility to ASD, pharmacological treatments, early intervention, and risk and protective factors for ASD.

In January 2009, the IACC released the first edition of its Strategic Plan for Autism Spectrum Disorder Research. The Strategic Plan advises Federal agencies and Congress on needs and opportunities in ASD research. The scientific community, service providers, advocates, parents, and people with ASD contributed to the Plan. The Plan has six sections focused on six critical questions asked by people and families living with ASD:

- When should I be concerned?
- How can I understand what is happening?
- What caused this to happen and can this be prevented?
- Which treatments and interventions will help?
- Where can I turn for services?
- What does the future hold?

The NIH ACC plays an integral role in coordinating NIH activities inspired by and relevant to the Strategic Plan. Consistent with the Strategic Plan, the six ACE centers and five networks that comprise the ACE program have begun research on biomarkers, genetic susceptibility to ASD, pharmacological treatments, early intervention, and risk and protective factors for ASD.

**Description of Disease or Condition**

Leo Kanner first described autism in 1943 as a disorder “characterized by extreme aloneness and a desire for the preservation of sameness, with a variety of behavioral (cognitive, affective) symptoms derived from them.” Over time, growing recognition of a broader range of related disorders led to the use of the term autism spectrum disorders (ASD), which includes several complex neurodevelopmental disorders of early childhood that vary in severity, share common clinical features, and persist throughout the lifetime of the individual. Common features include social impairments; verbal and nonverbal communication difficulties; and restricted, repetitive, and stereotyped behavior patterns. “Classic” autistic disorder is the most disabling; other forms of ASD, such as Asperger’s disorder, have fewer or milder symptoms. Intellectual disabilities, seizures, and self-abusive behaviors are common among children at the more severe end of the spectrum.

A child’s primary caregivers often are the first to identify ASD symptoms. As early as infancy, a baby with ASD may be unresponsive to people or focus intently on one item to the exclusion of others for long periods. A child with ASD may appear to develop normally and then withdraw and become indifferent to social engagement. Clinicians can make a reliable ASD diagnosis for most children by age 3. The current ASD diagnostic criteria and classifications represent progress in identifying a core set of developmental symptoms that, in the past, clinicians might have diagnosed differently because the criteria were more narrowly defined than they are today.

**Burden of Illness**

ASD causes tremendous economic and social burdens for families and society at large. Although ASD varies greatly in character and severity, it occurs in all ethnic and socioeconomic groups and affects every age group. Currently, no coherent and comprehensive system of care is available for affected individuals. People with ASD might receive private and public services in special education settings, hospitals, university medical centers, or residential treatment facilities, among others.

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Some scientists and economists have estimated that the combined direct and indirect costs of providing care for all Americans with ASD during their lifetimes exceed $34 billion. The estimated costs over a lifetime for each person total $3 million.

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Families often incur large debts for medical and education services that public programs or medical insurance do not cover. In addition, autism often leads to profound emotional hardships for patients and their families.

CDC currently estimates that as many as 9.0 per 1,000 children have an ASD. The total number of individuals in the United States with an ASD diagnosis is unknown. However, CDC estimates that up to 730,000 individuals age 21 or younger have an ASD (assuming a prevalence rate of 1 in 110, a birth rate of 4 million children per year in the United States, and a constant prevalence rate over the past 20 years). Boys are approximately four times as likely as girls are to have an ASD.

Prevalence estimates, or the number of affected individuals at a given point in time, have increased markedly since the early 1990s. However, it is unclear if incidence, the number of new cases across time in the same population, also has increased. It also is unclear whether the rise in prevalence is due to such factors as the use of different criteria to diagnose ASD or earlier and more accurate ASD diagnoses. A similar increase in ASD prevalence has occurred in other countries.

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**Scope of NIH Activities: Research and Programmatic**

The six centers and five networks that compose the ACE program cover a broad range of ASD research areas, including early brain development and functioning, social interactions in infants, rare genetic variants and mutations, associations between autism-related genes and physical traits, possible environmental risk factors and biomarkers, and a potential new treatment.

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In the past, ASD researchers collected clinical data using different formats and analysis methods and stored data in different locations. This approach made comparing data from different sites difficult. ASD researchers now can use the National Database for Autism Research (NDAR), a common bioinformatics system, to gather and analyze data from human subjects. The NDAR has built on the collaborative aspects of the STAART data coordinating center and makes gathering, evaluating, and sharing ASD research data from a variety of sources easier and faster for researchers. NDAR allows the seamless integration of data, research tools, and research projects from institutions across the United States and internationally.

All ACE centers and networks are contributing data to NDAR. In addition, efforts to add data from the STAART data coordinating center are underway. NDAR also will coordinate data access with other Federal databases, such as the NIMH Center for Collaborative Genetic Studies. The center is a national resource for researchers who study the genetics of complex mental disorders, including ASD, and stores human DNA, cell cultures, and clinical data.

**NIH Funding for FY 2008 and FY 2009**

Three NIH ICs fund the ACE program—NICHD, NINDS, and NIMH. Actual NIH funding for the ACE program, which includes centers (P50s), a cooperative agreement (U01), and networks (R01s), was $25.2 million in FY 2008 and $26.5 million in FY 2009, including $1.89 million from ARRA funds.

**FY 2008 and FY 2009 Progress Report**

**Programmatic and Research Activities and Outcomes**

Several accomplishments of the ACE program and one of the STAART centers (funded through 2008) are highlighted briefly below.

- Researchers at Yale University are searching for biomarkers of visual engagement and auditory perception in infants at risk for ASD.
- Researchers at the University of Illinois at Chicago are studying genetic factors as well as brain chemicals and brain functions that could account for repetitive behaviors in people with ASD. They also are testing whether genetic differences influence how individuals respond to certain medications intended to reduce the frequency of these behaviors.
- Researchers at the University of Washington are investigating genetic and other factors that might increase a person’s risk of having an ASD and factors that might protect people from getting an ASD.
- Investigators involved in the University of North Carolina at Chapel Hill ACE network are studying abnormal processes in early brain development by examining brain images of very young children at risk for developing ASD.
- The University of California, San Diego, ACE is using brain imaging methods to track brain development in children believed to be at risk for ASD. The researchers aim to identify brain or other physical differences that might increase a child’s risk of developing ASD.
- Researchers at the University of California, Los Angeles, are determining the causes and treatments of social communication problems in people with ASD.
- The University of Pittsburgh ACE is studying how people with ASD learn and understand information.
- Researchers at the Drexel University network sites are studying possible risk factors and biological
Researchers at the Drexel University network sites are studying possible risk factors and biological indicators of ASD before and soon after birth. This project is part of the Early Autism Risk Longitudinal Investigation (EARLI).

• Researchers at the University of California, Davis, network sites are examining factors that might be useful for improving treatment outcomes in very young children with autism. They are comparing an intensive behavioral intervention to standard community-based treatment.

• Investigators at Wayne State University network sites will conduct a clinical trial to test the safety and efficacy of buspirone, a drug that increases the body’s production of serotonin—one of several neurotransmitters that brain cells use to communicate with each other—as an early intervention in children younger than 6 years with ASD. A pilot study by the Wayne State researchers showed that buspirone improves social interaction and reduces repetitive behaviors, sensory dysfunction (extreme sensitivity or lack of sensitivity to light, noise, and touch), and anxiety in children with autism.

• Investigators at Wayne State University network sites will conduct a clinical trial to test the safety and efficacy of buspirone, a drug that increases the body’s production of serotonin—one of several neurotransmitters that brain cells use to communicate with each other—as an early intervention in children younger than 6 years with ASD.

• Researchers at the University of California, Los Angeles, network sites are studying the relationship between genes related to autism and physical features. They also are investigating rare genetic variations, mutations, and abnormalities that affect a person’s risk for autism.

• In three separate studies of genetic risk factors linked to ASD, STAART investigators, ACE investigators, and other collaborators identified common and rare genetic factors that affect ASD risk. The results point to genes that are involved in forming and maintaining the connections between brain cells. These results confirm previous findings on the role of genes in ASD and abnormal brain wiring in people with ASD. The study findings are a significant step forward in a larger effort to understand the complex genetic architecture of ASD. The investigators recently published their findings in the journals Nature, 53, 54 and Annals of Human Genetics. 55

• STAART investigators collaborated in a multisite study to evaluate the efficacy of a drug, citalopram, to treat ASD symptoms. Citalopram selectively can inhibit the activity of serotonin, which might play a role in the repetitive behaviors associated with autism. The researchers recently published their results in the Archives of General Psychiatry. 56 After 12 weeks of treatment, roughly one out of three children in both the group that took citalopram and the group that took a placebo (medicine with no active ingredients) had fewer or less severe repetitive symptoms. However, the children in the citalopram group experienced more adverse side effects than the children in the placebo group. According to the researchers, the study results show that the drug is no better than placebo in treating ASD symptoms.

Recommendations for Improving the Effectiveness, Efficiency, and Outcomes of the Autism Centers of Excellence

Evaluation Plans

The Combating Autism Act of 2006 and the NIH Reform Act of 2006 require NIH to evaluate the performance and research outcomes of the ACE program. In 2008, NIH established a trans-NIH evaluation team to conduct the first evaluation, which will gather baseline, descriptive data on the implementation of the program. The evaluation will use a two-part approach, focusing on process evaluation questions related to program implementation and determining the feasibility of future evaluation efforts to assess the outcomes of the ACE program.

In 2010, HHS will provide Congress with a progress report on activities related to ASD that will include results from the initial ACE program evaluation. The report also will discuss the incidence of ASD, average age at diagnosis, average age of intervention start, effectiveness and outcomes of interventions by subtype, and effectiveness and outcomes of newly developed intervention strategies.

Future Directions

In 2010, the NIH ACC plans to convene a 2-day meeting at which the investigators will present the goals of their ACE and exchange ideas for collaborations. Some sessions will address data sharing options through the NDAR, with time allotted for a question-and-answer period with NDAR staff. ACE principal investigators and project principal investigators, as well as core directors and data managers, will be invited to attend. Principal investigators will be encouraged to invite K award (career development grant) recipients, fellows, and postdoctoral students from their laboratories. Approximately 55 to 65 ACE investigators are expected to attend this meeting, which will take place annually thereafter.

Table 4-6. Studies to Advance Autism Research and Treatment (STAART) Centers

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<tr>
<th>Institution and Location</th>
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<tbody>
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<td>University of North Carolina, Chapel Hill, NC</td>
<td>2002</td>
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<td>Boston University, Boston, MA</td>
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<td>Kennedy Krieger Institute, Baltimore, MD</td>
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<tr>
<td>Mt. Sinai Medical School, New York, NY</td>
<td>2003</td>
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<tr>
<td>Institution and Location</td>
<td>Year Established</td>
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<tr>
<td>University of California, Davis, CA</td>
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