Multi-Million Autism Center of Excellence Established at UC San Diego

NIMH grant will fund groundbreaking research on the causes, early identification and treatment of autism

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One of six Autism Centers of Excellence (ACE) in the country has been established at the University of California, San Diego by the National Institutes of Health (NIH), to be directed by Eric Courchesne, Ph.D., professor of neurosciences at the UC San Diego School of Medicine and a leading expert on brain abnormalities associated with autism, a brain disorder affecting an estimated two million people in the U.S. The symptoms are impaired social, emotional, language and cognitive development.

Funding for the Center is expected to be more than $10 million. With this grant, the UC San Diego ACE hopes to create a "signature" of autism that will allow for earlier diagnosis and intervention by integrating behavioral, developmental and biological findings.

"Most importantly, we hope to find biomarkers of autism during infancy, so that targeted interventions can begin as early as possible to improve brain function and behavior in autistic children," said Courchesne.

Autism is the fastest-growing developmental disability, and its frequency appears to be on the rise, affecting nearly one in every 150 births. Funded by the National Institute of Child Health & Human Development, the National Institute of Deafness and other Communication Disorders, the National Institute of Environmental Health Sciences, and the National Institute of Neurological Disorders and Stroke, the UC San Diego Autism Center will focus on the earliest stages of brain development, both function and growth; behavioral therapy, and genetic components related to autism in infants.

Infants at risk and toddlers throughout San Diego will be identified to participate in the study. The project will include behavioral intervention for autistic children who enroll in studies through the Center.

"Our research team will focus on uncovering causes of the disorder, finding the most beneficial behavioral treatment, and, long term, identifying possible biologically based treatments," said Courchesne.

"The fact that UC San Diego was awarded this grant is further proof of the great work in science done at the university. The autism research done at UCSD will no doubt instill hope in the hearts of millions of families who are living with autism," said Congresswoman Susan Davis, a cosponsor of the Combat Autism Act passed in 2006 by the U.S. Congress to address "an epidemic of autism."

The Autism Centers of Excellence awards were made possible by this legislation, which doubled federal funding of research in the disease. Although it is a highly heritable disorder, the genetic causes for it are poorly understood.

The innovative research at the UC San Diego Autism Center will build on Courchesne's discovery that autism involves sudden, excessive brain growth during the first year of life.

"Such abnormal brain growth very likely triggers autistic behavior in infants and toddlers, so the new UCSD Autism Center of Excellence aims to discover the genetic bases of this early brain overgrowth," said Courchesne, who is also director of Rady Children's Center for Autism Research and whose work has been supported over the years by Rady Children's Hospital. The research team will seek to pinpoint the exact regions of the infant brain that are growing and functioning abnormally by conducting sophisticated brain imaging studies on infants at risk for autism during natural, non-sedated sleep.

The UCSD program will also be the first NIH-sponsored effort to use genetics and brain growth information to guide neural stem cell research on autism, with the hope of identifying potential bio-therapeutics that could benefit infants with autism in the future.

The UCSD Autism Center will include collaborators from the UC San Diego campus, The Salk Institute, The Scripps Research Institute, the University of Syracuse, and Rady Children's Hospital and Health Center, affiliated with UC San Diego's department of pediatrics. **Detecting Risk at an Early Age**

"Ours is the first study of the biology of autism in infancy," said Courchesne. This groundbreaking look at the early biological abnormalities in autism is possible because of a novel approach to studying infants who are at risk for autism, developed by Center co-investigator Karen Pierce, Ph.D., of UC San Diego's department of neurosciences. Called the "One Year Well-Baby Check-Up Approach," this unique approach recognizes the vital importance of the pediatrician, giving the physician a fast, inexpensive and practical procedure for identifying 12-month olds who may be at risk for developing autistic behavior.

The procedure is designed to identify children who are missing significant social milestones by their one-year checkups by uncovering warning signs such as lack of eye contact or interest in the parents' faces, reduced pointing at objects, lack of response to parents' voices, or reduced curiosity in exploring toys and other objects. A large number of San Diego area pediatricians have been trained in this procedure and, through their participation, the at-risk infants they identify will be referred to the new UCSD Autism Center of Excellence for free evaluations. Participating pediatricians represent UC San Diego, the Childrens Primary Care Medical Group, Kaiser Permanente, Scripps Mercy, Scripps Clinic, La Jolla Pediatrics, the Naval Medical Center, and Sharp Rees-Stealy Medical Group.

Infants and toddlers participating in the five-year study will also be tested for physiological and neural abnormalities, including genetic tests designed to pinpoint the particular genes involved in autism.

"Biomarker discovery and early identification of autism can facilitate the development of very-early intervention methods that could greatly enhance positive outcomes for toddlers with the disorder," said Courchesne. "Our work opens up an entirely new field of study that we hope will eventually lead to new therapeutics that could minimize or stop the abnormal brain growth, thereby enabling each child to live a more normal life."

Behavioral Intervention

Parents and their children will also receive free and intensive in-home behavioral treatments for a period of one year. Therapy for each autistic child will involve 15 hours a week of social, play-based training, and parents will learn how to enhance their autistic child's language and social behavior.

"We use a combination of scientifically validated behavioral treatments - for example, pointing and showing behaviors related to building social attention skills in toddlers," said Laura Schreibman, Ph.D., UCSD professor of psychology and world leader in the behavioral treatment of autism, who is director of the behavioral therapy core of the new UCSD Autism Center. "Trained therapists go into the home to work with parents to teach their babies how to socially communicate, explore their environment and increase the babies' motivation to learn new things."

Biology and Genetics

Another major component of the project is to uncover biological information on how genes are related to brain overgrowth. Courchesne's past study, which was published in the *Journal of the American Medical Association* (JAMA) and received world-wide attention, showed that, in autism, head circumference at birth is near normal. It then increases at an abnormally accelerated rate, often becoming larger than normal by 12 months of age, just when the first "red flags" warning of possible autism may also appear. Courchesene's discovery has been confirmed by a number of recent studies by independent research groups.

Currently, there is little information about which genes are responsible for the abnormal brain growth and early behavioral symptoms in autism. In order to identify such genes, projects in the Center - headed by Anthony Wynshaw-Boris, M.D., Ph.D., UCSD professor of pediatrics and psychiatrist Steven Glatt, Ph.D., at the University of Syracuse- will study genes and their level of expression during this critical early period from 12 months through 36 months of age.

"Our DNA testing will be based on the brain-overgrowth hypothesis, focusing on genes that impact either cell growth or cell death in the brain," said Wynshaw-Boris. "By viewing autism through the lens of a single hypothesis, the research team hopes to shine a light on cause and treatment of the disease."

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