seaver autism center for research & treatment @ mount sinai

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WELCOME

to our introductory issue of the Seaver Autism Center Newsletter. We will be bringing you timely updates about new developments related to research and treatment of autism spectrum disorders, as well as activities at the Seaver Autism Center. Please email SeaverCenterEditor@mssm.edu to be placed on our mailing list for future issues.

IN THIS ISSUE

Meet the Director

DR. JOSEPH BUXBAUM IS A WORLD-renowned molecular geneticist who has been closely affiliated with the Seaver Autism Center since joining the faculty at Mount Sinai in 1997. Dr. Buxbaum was recruited in part to establish a research program in molecular genetics in autism spectrum conditions within Mount Sinai. As such, he was Director of Molecular Genetics in the Seaver Autism Center for seven years, and took over the Directorship of the Seaver Autism Center itself in 2008. Dr. Buxbaum has focused on understanding the molecular and genetic basis of autism spectrum conditions, which will allow for a better understanding of the etiology of such disorders, and lead to the development of novel therapeutics for the negative aspects of these conditions.

Dr. Buxbaum heads the Laboratory of Molecular Neuropsychiatry, which has taken the findings regarding the causes of autism and translated them into animal models where therapeutic approaches can be evaluated. In this context, Dr. Buxbaum has established the Autism Model Systems Initiative, which makes use of multiple experimental systems to develop and evaluate novel therapeutics in autism spectrum conditions.

Collaborating with other independent sites ensures that the best science in the service of individuals and families is carried out. Dr. Buxbaum is a lead investigator in the Autism Genetics Consortium, the Autism Genome Project, and the Autism Case Control Cohort, and is a part of the Psychiatric Genetics Consortium. These large Consortia have the benefit of advancing the best science at the fastest pace and hence will best serve the families.

Dr. Buxbaum has received numerous awards for his research. He is the G. Harold and Leila Y. Mathers Professor; he has received recognition from the New York University Child Study Center for his "distinguished accomplishments and professional contributions to research in autism" (2004); from the American College of Neuropsychopharmacology in the form of the Daniel H. Efron award for "excellence in research in neuropsychophamacology" (2005); as well as most recently, from the Eden Institute Foundation for his "commitment and dedication to improving the quality of life in individuals with autism" (2008). Dr. Buxbaum has over 100 publications in esteemed journals to his credit and his work on autism and related conditions has been published in major journals, including *Nature, Nature Genetics, Proceedings of the National Academy of Sciences, Molecular Psychiatry,* and *Biological Psychiatry.* ■

Studies at the Seaver Autism Center for Research and Treatment

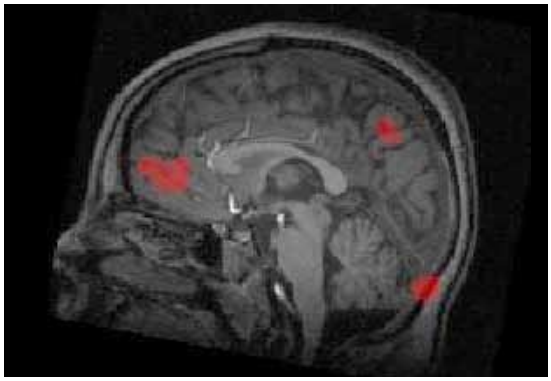
Autism spectrum disorders (ASD) are marked by significant impairments in social functioning and social cognition, language impairments, and repetitive behaviors. The Seaver Autism Center for Research and Treatment has ongoing research studies that are designed to advance knowledge in the field of ASD and apply that understanding to new treatment approaches. Below are summaries of current studies. Please contact the Seaver Autism Center at (212) 241-0961 or TheSeaverCenter@mssm.edu to learn more or to participate in a study.

FAMILY AND GENETIC STUDIES

The Autism Genome Project (AGP) is a large-scale collaborative project that aims to identify the genetic factors underlying autism. The Seaver Autism Center plays a lead role in the Autism Genome Project consortium which brings together researchers from over 50 centers across the United States, Canada, and Europe. The goal of this important project is to collect genetic and clinical information from a large sample of families with autism spectrum disorders in order to identify genetic risk factors and define the genetic architecture of ASD.

The Autism Simplex Collection (TASC) is an international study that is committed to making materials available to qualified researchers who are studying the causes and treatments for autism and ASD. TASC is planning to enroll 2000 trios, including a child with ASD and both parents, into this important initiative. Participants give a small sample of blood and are assessed by our clinical staff.

The Family Studies Research Program was developed to better understand the familiality of autism symptom domains and how autism-related difficulties with social interactions, communication skills and/or restricted and repetitive behaviors and interests may run in families. The program works with all available family members to assess behavioral traits of ASD and attempt to locate genes associated with these characteristics in individuals with autism and their families.



Functional Magnetic Resonance Imaging scan of brain activity during a social language task in a child with autism spectrum disorder

Investigating Autistic Traits and their Connection to Oxytocin and Cholesterol is a study that assesses children with ASD between the ages of 6 and 16 and their first-degree family members. Recent findings suggest that low levels of oxytocin and deficiencies in cholesterol synthesis may be related to symptoms of ASD. This study investigates the relationship between traits of autism, oxytocin, and cholesterol.

CLINICAL TRIALS

Social Skills Groups for Children is designed to evaluate changes in behavior and in the brain associated with social skills treatment in children with ASD ages 8 to 11 years old. While social skills

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The Clinical Program at the Seaver Autism Center

Our Clinical Program offers *Assessment and Evaluation Services,* including genetic, diagnostic, neuropsychological, and academic testing, and psychiatric evaluations. In addition, we offer *Comprehensive Treatment Services,* including medication management, social skills groups, parent training sessions, cognitive behavior therapy, and a sibling support program. And as part of our commitment to education and community care, we also have a *Community Outreach & Training Program* that provides lectures and workshops to parent groups, agencies, and schools. Finally, the Seaver Autism Center hosts an annual conference to address current scientific trends and discoveries. ■

Studies

Continued from previous page

groups are widely used, little is known about the efficacy of these treatments in ASD. This study compares two commonly used approaches to social skills groups – a play-based approach and a cognitive behavioral approach. We use tests of social functioning as well as neuroimaging to examine changes in both social behavior and activity in the brain following treatment.

A Randomized Double Blind Placebo Controlled Trial of CM-AT™ examines the effect of an investigational product to assess the impact on hyperactivity and other symptoms of ASD in children 3 to 8 years old. A significant proportion of individuals with ASD suffer from gastrointestinal problems and many have self-imposed dietary restrictions as a result. This study explores the hypothesis that undigested protein in the gastrointestinal system can contribute to behavioral symptoms of ASD and is designed to assess whether adding a novel formulation to potentially aid in digestion will improve ASD symptoms, after pancreatic insufficiency is established by a stool test.

An Open-Label Study of Trichuris Suis Ova (TSO) for the Treatment of Adult Autism Symptom Domains is designed to assess the efficacy of a porcine whipworm on autism symptoms. There is a significant amount of evidence to suggest that patients with autism and their families have higher rates of immune system dysfunction, which may be associated with symptoms of ASD. In this study, TSO are ingested by adults with ASD, eggs hatch in the gastrointestinal system and potentially activate the immune system against the whipworm to promote a more adaptive immune response and reduce the proliferation of inflammatory immune molecules.

NEUROIMAGING

Informational and Neural Bases of Empathic Accuracy in Autism Spectrum Disorder examines how people with ASD use different types of information in a social context to understand what other people are feeling. In the Empathic Accuracy test, participants attempt to identify the real emotions of people in videos while undergoing a functional MRI (fMRI) scan. In addition to Empathic Accuracy, this study also examines two more basic components of social information processing: the Mirror Neuron System and the Reward System. The Mirror Neuron System is thought to provide a neural mechanism for understanding the actions, intentions, and emotions of others, and the Reward System helps us understand the role of social reward in modulating implicit learning.

The Effects of Oxytocin on Social Cognition in Autism Spectrum Disorders examines the critical role that oxytocin plays in social behavior and social cognition in adults with ASD. Oxytocin may be a promising candidate to target the social deficits in ASD. This study uses intranasal oxytocin in conjunction with fMRI to investigate the acute effects of oxytocin on empathic accuracy, a novel and ecologically valid measure of complex social cognition, the mirror neuron system, and social reward.

The Neural Basis of Sensory and Perceptual Symptoms in Autism examines the sense of touch in adolescents with ASD aged 12-17 years old using fMRI. This study investigates the neural pathways that mediate sensory-perceptual abilities in ASD to assess brain activity in response to self-produced tactile stimulation and to better understand the sensory sensitivities seen in ASD.

OTHER STUDIES

Autism Spectrum Disorders Risk Alert (ASDRA) is an online and medical education tool designed to teach pediatricians how to recognize early warning signs of ASD. This study is creating an integrated web based toolset with a video-intensive database. Children 12 months to 3 years-old with ASD are compared to typically developing children using video to create this educational tool and facilitate the early assessment of ASD.

Mediators of Motor Skills in Adolescents and Adults with ASD is a study that compares the motor functioning of three groups of adults ages 18-40. The groups include individuals with high functioning autism or Asperger's disorder, Attention Deficit/Hyperactivity Disorder, and individuals without disabilities. Factors that influence performance on motor tasks such as attention, organizational skills, and memory are also evaluated. ■

Genetics in the Service of Patient Care

WITHIN THE PAST YEAR there have been major changes in the understanding of the etiology of autism spectrum disorders (ASD). The Seaver Autism Center has been a founding site of several large genetic groups, including the Autism Genome Project (AGP) and the Autism Case Control (ACC) study. These initiatives have identified several new causal genetic areas of focus underlying specific cases of ASD. This has led to a profound shift in our thinking, such that ASD can now be conceived of as having multiple independent causes. In many cases the cause can be largely attributed to a specific causal event. This perspective raises both great challenges and great

opportunities. One challenge is that the complexity may necessitate studying and/or treating different forms of ASD differently. The opportunities are that with these rare causal variants, it becomes possible to give a medical diagnosis for some cases of ASD, to have more predictive power regarding risk of recurrence in siblings, and to think about novel targeted therapeutic approaches.

As an example from recent work carried out at the Seaver Autism Center, we identified the cause of ASD in a boy as a novel mutation in the *PTEN* gene. Once this mutation was identified, it could be concluded that this was the cause of the ASD, which immediately led to genetic counseling opportunities. The mother of the child was pregnant but, once she was informed by genetic counselors that the mutation in her affected child occurred spontaneously and would not recur, her concern about her unborn child was ameliorated.

A dramatic example appeared in the recent large-scale clinical trial in Fragile X Syndrome (FXS). FXS accounts for approximately 2% of ASD cases. Detailed analysis of mouse and other models of FXS gave rise to a hypothesis that over-expression of a glutamate receptor in the synapse underlies some of the cognitive deficits in the disorder. As a result of this hypothesis, drugs that targeted this receptor were tried in mice and other model organisms that had mutations that mimic FXS, and these drugs were shown to correct some of the cellular and behavioral deficits observed in the mice. Since January 2008, there have been large-scale clinical trials in FXS following these animal studies.

GENETIC TESTING AT THE SEAVER AUTISM CENTER

In recognition of these advances and an ever-changing field, we have introduced state-of-the-art genetic testing to clinical practice and research at the Seaver Autism Center. As part of this, we have partnered with the Department of Genetics and Genomic Sciences and the Institute of Personalized Medicine at Mount Sinai School of Medicine to translate the research findings from the Seaver Autism Center and from other laboratories around the world into genetic tests to supplement behavioral assessments in ASD. The Seaver Autism Center has always positioned itself to be a leader in defining the standard of care in ASD. It is our vision that using state-of-the-art molecular genetic, neurobiological, and clinical resources, we are now posed to make significant breakthroughs in identifying genetic subtypes of ASD and developing targeted treatments.

To learn more about our current studies, please see the related article in this issue. ■

This article was adapted from the Spring 2009 issue of Autism Spectrum News *and can be viewed at www.mhnews-autism.org.*

PHOTOGRAPH: MATTHEW SEPTIMUS