



Recent Findings from Research at the Seaver Autism Center

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NEW MOUSE MODEL FOR AUTISM

A team of researchers, led by Joseph Buxbaum, PhD, Director of the Seaver Autism Center, created and studied a mouse model that has a loss of one copy of the SHANK3 gene. The team discovered that nerve cells communicate less effectively when one copy of the SHANK3 gene is missing. In addition, missing a copy of this gene hinders normal nerve-cell learning processes. This finding could explain how the loss of a copy of SHANK3 contributes to the behavioral manifestations of autism and the related Phelan-Mc-

Dermid Syndrome. Dr. Buxbaum said, “Armed with this information, we are beginning to test drugs in these mice that are aimed at treating the syndrome at its root cause, improving nerve cell communication.”

“We hope and expect that, like other developmental disorders such as Fragile X syndrome, the use of mouse models will lead directly to clinical trials that can benefit patients.”

The team from Mount Sinai included Ozlem Bozdagi, MD, PhD, Takeshi Sakurai, MD, PhD, Patrick Hof, MD, and Qiang Zhou, PhD, as well as Jacqueline Crawley, PhD, of the National Institutes of Health.

Dr. Buxbaum explains, “We know that the SHANK3 mutation plays a central, causative role in forms of autism and in Phelan-McDermid Syndrome, but we wanted to learn

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The First International Phelan-McDermid Syndrome (PMS) Foundation Symposium was recently co-hosted by the Foundation together with the Seaver Autism Center. Scientists, clinicians, and parents of children with PMS came together to discuss active research and progress in the development of novel therapeutics for people with PMS. Presenting from the Seaver Autism Center was Ozlem Bozdagi Gunal, MD, PhD, who discussed initial results of a biological treatment in a model system of PMS. Joseph Buxbaum, PhD moderated a roundtable discussion. More information about topics discussed at the Symposium can be found at www.shank3gene.org.

“Oxytocin is widely believed to make all people more empathic and understanding of others. Our study contradicts that. Instead, oxytocin appears to be helpful specifically for those who are less socially proficient.”

more about how it does this.” Mice were genetically engineered to lack one copy of *SHANK3*—comparable to patients who have a *SHANK3* mutation on one copy of the gene. The team analyzed both nerve cell and brain activity, and examined social behaviors in the mice.

The researchers identified impaired nerve cell communication in the *SHANK3* group, and noted that the nerve cells and synapses experienced altered functional and structural plasticity. At the Laboratory of Behavioral Neuroscience at the NIH, Dr. Crawley observed a decreased level of social interaction between male and female *SHANK3* mutant mice.

“These results have helped us identify a pathological mechanism behind the neurobehavioral manifestations of autism and related syndromes,” said Dr. Buxbaum. “We hope and expect that, like other developmental disorders such as Fragile X syndrome, the use of mouse models will lead directly to clinical trials that can benefit patients.”

A report of this study is available for free through the open-access journal *Molecular Autism* at the following link: <http://www.molecularautism.com/content/1/1/15/abstract>.

This study was sponsored by the Seaver Foundation, a special multi-investigator grant given to co-authors Drs. Buxbaum, Crawley, Hof and Zhou from the Simons Foundation, and by a generous gift from Paulina Rychenkova, PhD, and William Gibson.

HORMONE OXYTOCIN IMPROVES SOCIAL COGNITION

The role of oxytocin has received quite a bit of attention recently. In one study conducted by researchers at the Seaver Autism Center and Columbia University, it was found that this naturally-occurring hormone enhances the social cognitive abilities for individuals who have diminished social perception skills. However, the hormone has little or no effect on those who are more socially proficient. Jennifer Bartz, PhD, Assistant Professor of Psychiatry, and lead author of the study, said, “Oxytocin is widely believed to make all people more empathic and understanding of others. Our study contradicts that. Instead, oxytocin appears to be helpful specifically for those who are less socially proficient.”

In the research team’s randomized, double-blind, placebo-controlled, cross-over challenge, they gave 27 healthy adult men intranasal oxytocin or a placebo. The participants of the study then executed an empathic-accuracy task.

Though none of the participants had autism, Dr. Bartz and her team determined whether each man’s level of social proficiency affected his reaction to a dose of oxytocin differently. The researchers used the Autism Spectrum Quotient (AQ) in order to predict the men’s social cognitive performance. They predicted that oxytocin would work best for those men with higher AQ scores, and therefore lower social proficiencies.

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Seaver Center Athletes

The Seaver Autism Center is proud to join with the Singer family and [Team Drive4Rebecca](#) in the New York City Triathlon on August 7, 2011. Half of all the money raised by the Seaver Autism Center’s Team will go to the Center to support active research, while the other half will be donated to Drive4Rebecca’s continuing projects.

Help us cheer on our Seaver athletes!

Visit <http://www.crowdrise.com/TeamDriveForRebecca/fundraiser/seaverautismcenter>.

Recent Findings *Continued from previous page*

The results of the study, published in *Psychological Science*, confirmed the researchers' hypothesis. "Our data show that oxytocin selectively improves social cognition in people who are less socially proficient, but had little impact on more socially proficient individuals," Dr. Bartz said. The men who were originally more socially proficient remained that way, and scored well on the empathic accuracy task whether they received oxytocin or the placebo.

The participants who were originally less socially proficient scored poorly if they had been given the placebo but significantly better if they had been given oxytocin, so much so that their scores matched those of the more socially proficient men. Dr. Bartz said, "While more research is required, these results highlight the potential oxytocin holds for treating social deficits in people with disorders marked by deficits in social functioning, such as autism."

This important research was covered by several media outlets, including an interview with Dr. Bartz and Jon Hamilton on National Public Radio (NPR) News during the Health section of the Morning Edition on Jan. 3.

Dr. Bartz and her colleagues have received a grant through the National Institute of Mental Health to continue their research on the impact of oxytocin beyond this study, specifically in adults with ASD. ■

News & Events

► JOEL ELKES RESEARCH AWARD

Dr. Buxbaum was recently awarded the prestigious Joel Elkes Research Award from the American College of Neuropsychopharmacology (ACNP). Every year the College presents this award to a scientist who has made a significant

clinical or translational contribution to neuropsychopharmacology.

► TEXTBOOK OF AUTISM SPECTRUM DISORDERS

The new *Textbook of Autism Spectrum Disorders*, co-edited by Dr. Alexan-

der Kolevzon, covers available treatment approaches for autism spectrum disorders (ASDs) and is designed for practitioners, as well as parents of individuals with ASDs who are looking to understand biomedical and behavioral treatment options. The textbook is available on www.amazon.com.



Dr. Buxbaum (center) receiving his award from (left) Dr. David Braff, Chair, 2010 ACNP Honorary Awards Committee & Past President (2009) and (right) Dr. David Rubinow, 2010 ACNP President.

► UJA FACULTY LINE, AUTISM COMMUNITY CONSULTATION

Michelle L. Gorenstein-Holtzman, PsyD, returned to the Seaver Autism Center team to join the clinical faculty and serve as a liaison between the UJA Federation and the Seaver Autism Center. Dr. Gorenstein-Holtzman is consulting with community agencies on social and recreation programming for children with ASDs, including a new consultation relationship with the Brooklyn Autism Spectrum Disorders Initiative (BASDI) programs. Additionally, Dr. Gorenstein-Holtzman is arranging and providing staff training and par-

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Seaver News

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ent workshops related to research in ASD.

Dr. Gorenstein-Holtzman was most recently a Postdoctoral Fellow at Premier Healthcare in New York. Prior to that she was a Psy-

UJA Federation grant expands funding to support faculty line in community consultation

chology Intern at Mount Sinai. She received both her PsyD and MA in general psychology from Ferkauf Graduate School of Psychology at Yeshiva University.

SEAVER AUTISM CENTER ADVANCES IN AUTISM CONFERENCE

Please join us for the annual Seaver Autism Center Advances in Autism Conference on

SUNDAY, APRIL 3, 2011

We will feature a series of lectures and workshops led by many accomplished researchers:

Course Director

Joseph D. Buxbaum PhD
Director of the Seaver Autism Center

Alexander Kolevzon MD
Seaver Autism Center

Deborah A. Fein PhD
University of Connecticut

Declan Murphy MD
Kings College London

Latha Soorya PhD BCBA
Seaver Autism Center

Katherine Cody PsyD
Seaver Autism Center

Eric London MD
Autism Treatment Laboratory

Randall L. Carpenter, MD
Seaside Therapeutics

Dr. Stephen Shore, Ed.D., will give the Keynote Presentation, entitled "Life on and Slightly to the Right of the Autism Spectrum: An Inside View Towards Matching Best Practice to Needs." Dr. Shore will share his autobiographical story, and his presentation will also include a short activity demonstrating what it feels like to have autism.

*For more information, please contact Jessica Brownfeld at
jessica.brownfeld@mssm.edu*

*To register, please go to www.mssm.edu/cme/courses/autism
or contact Jeanette Cotto at jeanette.cotto@mssm.edu*

Ongoing Research

PHELAN-McDERMID SYNDROME

- This study is designed to comprehensively evaluate subjects with 22q13 deletions/SHANK3 mutations clinically and genetically to fully characterize this syndrome and clarify the prevalence of ASD and other features. The overall goal of this work is to explore clinical heterogeneity and to develop meaningful outcome measures for use in clinical trials.
- Participants in this study have 22q13 deletions/SHANK3 mutations.

EFFECTS OF OXYTOCIN ON SOCIAL PERCEPTION IN ADULTS WITH ASDs

- This study examines the critical role that oxytocin plays in social behavior and social cognition in adults with ASD.
- Participants in this study are physically healthy adults (ages 18–45) who meet diagnostic criteria for ASD.

STUDYING THE EFFICACY OF SOCIAL SKILLS GROUP IN CHILDREN WITH ASDs

- This study is designed to evaluate changes in behavior and in the brain associated with social skills treatment in children.
- Participants in this study are children with ASD, ages 8–11.

If you would like more information about these studies, please contact Jessica Zweifach at 212.241.2826 or jessica.zweifach@mssm.edu.

• **THE SEAVER AUTISM CENTER NEWSLETTER** brings you timely updates about new developments related to research and treatment of autism spectrum disorders, as well as activities at the Seaver Autism Center. To be placed on our mailing list, please contact SeaverCenterEditor@mssm.edu or The Seaver Autism Center, Mount Sinai School of Medicine, One Gustave L. Levy Place, Box 1668, New York, NY 10029. Our phone number is 212.241.0961 and our web site is www.SeaverAutismCenter.org.

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