seaver autism center
for Research & Treatment at Mount Sinai
NEWS

The Seaver Center's 27th Annual Advances in Autism Conference

We would like to thank the 640 attendees, hailing from 32 states and 22 countries, who tuned in to our 27th annual Conference on May 23. The focus of the event was precision medicine in profound autism.

We had the honor of featuring seven wonderful speakers who presented a wide variety of developments across the field of autism research, including breakthroughs in genetic discoveries as well as progress made toward obtaining novel pharmaceutical therapeutics.

The presenters also acknowledged challenges that they expect the field to face over the next few years in the pursuit of these pharmaceutical interventions, and how we may overcome them.

As Dr. Timothy Yu said, we, as a field, are "charging up the path of genetically caused disorders – one gene, one patient, and one disorder at a time."

You can access the recordings of each presentation, as well as the all-speaker panel, at: https://media.rampard.com/20230523/

Seaver in the Community

Brain Fair

The Seaver Center participated in the 11th Annual Brain Fair at Mount Sinai on March 14th. The event is organized by MiNDS (Mentoring in Neuroscience Discovery at Sinai), and consists of educational activities sponsored by various neuroscience-related departments across Mount Sinai. The goal is to facilitate learning about the brain for children and community members. The Seaver Center created an interactive puzzle with true-or-false questions about autism to help increase awareness and knowledge about the disorder.

ASF Day of Learning

On March 30, members of the Seaver Team had the opportunity to attend the Autism Science Foundation's 10th annual Day of Learning, of which the Seaver Center was a sponsor. Seaver Team member Ana Kostic, PhD, Director of Drug Discovery and Development gave a talk entitled *Next Steps for the Autism Ketamine Trials*. The Day of Learning was a wonderful way of to learn more about research findings in the field, and what issues are most pressing to families.

Autism Speaks 5K

Seaver Team Postdoctoral Fellows, Adele Mossa and Charikleia Chatzigeorgiou, represented the Seaver Center at the Autism Speaks 5K in Brooklyn on April 1. Adele came in 4th place and Hara came in 29th.
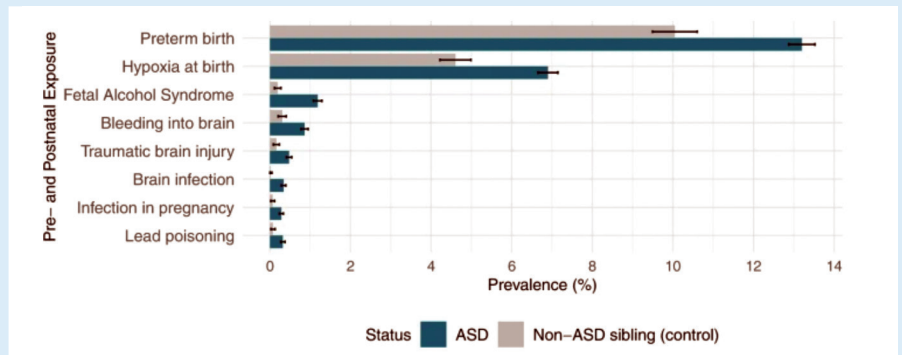

Publications

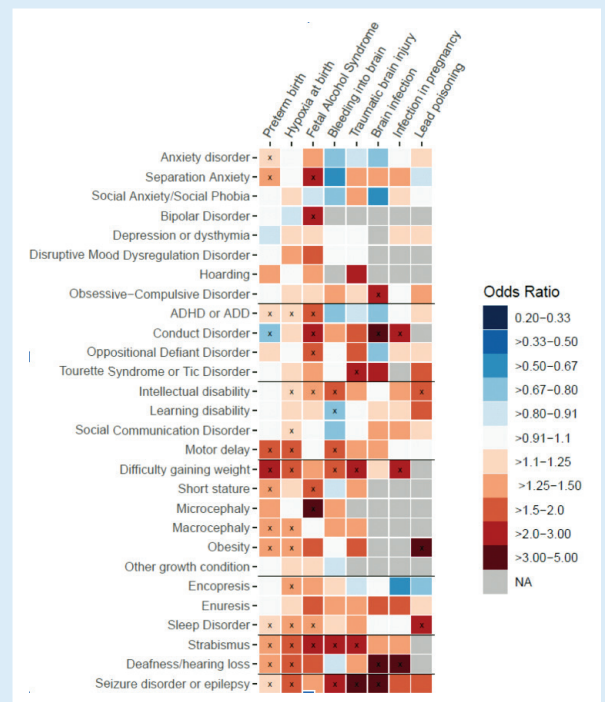**Comorbidities in Autism Spectrum Disorder and Their Etiologies**

A recent study led by Dr. Khachadourian from Dr. Janecka's lab from the Seaver Team, **"Comorbidities in autism spectrum disorder and their etiologies"**, was published in *Translational Psychiatry*, a peer-reviewed medical journal. Recent literature from the field suggests that 74% of individuals with autism experience comorbid conditions, the simultaneous presence of multiple diseases. With this study, the team sought to evaluate the possibility that these comorbid conditions may in fact be linked to specific pre- and post-natal exposures that are often associated with autism. A comparative analysis was also conducted in non-autism siblings as a means of more thoroughly assessing whether the pre- and post-natal exposures occur in conjunction to these comorbidities, independently of the presence of autism.

The figure below demonstrates that the burden of comorbidity is much higher in children with autism compared to their unaffected siblings, even once shared familial factors, like shared home environment or genetics, are accounted for by comparing siblings in the same families.
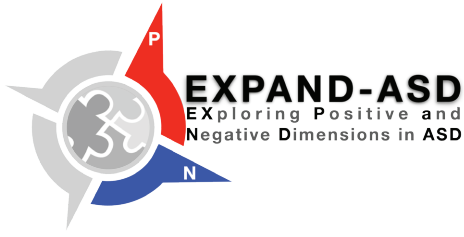

This figure demonstrates the way in which various comorbidities are not experienced at random, but rather, appear relative to certain perinatal exposures. Blue tiles on the figure below indicate medical conditions (vertical axis) that are less common in children with autism with certain perinatal exposures (horizontal axis), and red tiles indicate the opposite: that autism children with the exposure (e.g. preterm birth) were more likely to have the medical condition. Tiles with an asterisk indicate the associations that were statistically significant. Overall, the strongest associations were observed between brain injury/infection and epilepsy, brain or maternal infection in pregnancy and hearing loss, fetal alcohol exposure and microcephaly, and lead poisoning and obesity.

The researchers observed similar patterns of associations between early-life exposures and different medical conditions among the unaffected siblings of children with autism. These findings support the hypothesis that comorbidities in autism are associated with these pre- and post-natal exposures, irrespective of the diagnosis of autism itself.

The Foss-Feig Lab's New Diagnostic Questionnaire

The Foss-Feig research laboratory is working on developing a new questionnaire, the Positive and Negative Inventory (PNI) for ASD, for measuring autism symptoms in children between the ages of 3-11 years. The project is funded by an R01 from NIMH.

There is a large amount of variability in symptoms in autism. This phenomenon is challenging for clinicians and researchers, both for identifying autism within individuals, as well as for developing new treatments. Another consequence is that existing diagnostic questionnaires for autism are not effective in differentiating autism from other disorders. Many symptom descriptions are also vague. For example, two children with "difficulties forming social relationships" could be very different: one might not seek out friendships at all, while another might try

often and hard with little success. The PNI aims to capture these subtleties with more precise questions.

The PNI questionnaire is being tested by caregivers of 1,000 children with ASD and 400 children with typical development or with other developmental disorders such as ADHD or anxiety. At its completion, the questionnaire is expected to contain items that are very precise in their descriptive capturing of autism symptoms and useful for describing different subtypes of autism.

The Foss-Feig lab anticipates that this innovative, scientifically rigorous process will result in a much higher caliber assessment tool for autism, as compared to the current standard.

Over time, this research should have secondary benefits, including: 1) offering a new tool for assessing experimental therapeutics, 2) providing a new framework to test brain mechanisms and genetic contributions, and 3) contributing to more nuanced application of targeted treatment by offering a rapid, innovative, precise, and sensitive way to quantify differences in autism symptoms across children.

Congratulations, Michael!

Michael Flores joined the De Rubeis lab at the Seaver Center as an undergraduate at New York University, contributing to the lab's work on studying the role of DDX3X on cortical projection neurons in autism.

He recently accepted an offer to pursue a PhD in Neuroscience at the University of California, San Francisco, this coming fall. He was awarded a prestigious fellowship, the NSF Graduate Research Fellowship, which will cover 3 years of tuition as well as provide him with a stipend. While in graduate school, Michael intends to focus on the ways in which social experiences affect behavior and brain computations.

As part of the application process, he had to prepare a research proposal, for which he wrote about a hypothetical project about the molecular profile of cortical projection neurons that could be conducted at the De Rubeis lab.

He also had to write a personal statement, in which he described his experience of translating from Spanish to English for his mother when he was younger, and how that led to his work as a Spanish interpreter at NYU's Free Clinic during his time as a student.

His interests in translation and accessibility as part of healthcare have led to plans to explore science communication in graduate school.

Congratulations, Michael!

New Staff

MADISON CABALLERO, PHD
Madison is a bioinformatician working in the Mahjani lab studying the genetics of autism, particularly the role of rare and ultra-rare variation underlying the disorder and its comorbidities. She received her PhD from Cornell in 2022 and has a BS in Molecular biology from UConn. Outside of research, Madison enjoys theater and spending time with her cat.

CHIARA FIORENZANI
Chiara is an undergraduate student from the University of Bologna who recently joined the De Rubeis lab as an intern. Her research is focused on the molecular function of DDX3X in neurons. She is committed to advancing our understanding of the biological basis of mental health disorders through interdisciplinary approaches that bridge biology and computation.

HANNAH HAO, PHD
Hannah joined the labs of Dr. Jennifer Foss-Feig and Dr. Daniela Schiler in June as a Postdoctoral Fellow. She completed her PhD at Cornell University. Her research focuses on understanding the neural substrates involved in social interaction in individuals with autism, as well as exploring the impact of socio-demographic factors in this context.

EMMA HEMPSTEAD
Emma joined the Seaver Center in October 2022 as the Communications & Marketing Associate. Prior to that, she worked for the European Heart Journal as a Project Assistant & Medical Journalist. She graduated from Smith College in 2020 with a BA in English Literature & French Studies.

PARUL JAIN, PHD
Parul is a postdoctoral fellow working with the Foss-Feig and Schiller labs. She holds a B.Tech. in Computer Science and Engineering from IIT Delhi and a PhD in Physiology, Biophysics, and Systems Biology from Weill Cornell Medicine. She uses computational methods to understand the mechanisms of Misophonia and autism.

CANDICE MEDINA
Candice graduated from NYU in 2021 with a BA in Psychology. She is an Epidemiologist who joined the Janecka lab during her masters at Mount Sinai. After graduating in 2022, she stayed with the Janecka lab and currently serves as a clinical research coordinator. She has a background in and passion for working with underserved and underrepresented communities, and her research focuses primarily on healthcare disparities. Candice is currently applying to MD PhD programs.

Mount Sinai

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• SEAVER IS CONTINUING TO GO GREEN! Please send your email address to seavercentereditor@mssm.edu to receive this newsletter electronically.

DDX3X

The De Rubeis lab members

DDX3X syndrome is a rare neurodevelopmental disorder caused by mutations in the DDX3X gene, located on the X chromosome. DDX3X syndrome is one of the most common genetic causes of autism in females. The disorder was only identified in 2015.

Dr. Silvia De Rubeis leads a research lab that seeks to investigate the cellular and molecular mechanisms underlying DDX3X syndrome using mouse models. These studies help us understand how mutations in the DDX3X gene lead to developmental and behavioral deficits. Once these mechanisms are identified, it will be possible to work on developing novel therapeutics.

International DDX3X day is June 12th – this year, the De Rubeis lab would like the Seaver Community to know that we are beginning to understand how brain development changes when DDX3X is mutated, but we need your support to continue making progress and translating these discoveries into new treatments.

SAVE THE DATE

**SEAVER
CELEBRATION**

30 year anniversary
of the Seaver Autism Center

HONORING Dr. Alex Kolevzon

**THURSDAY
NOVEMBER 16TH**

More details to come