

NEWS

INSAR 2020, from home

BY SPECTRUM

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Like so many other events this year, autism's biggest annual conference — the International Society for Autism Research (INSAR) meeting — was forced to go virtual because of the coronavirus pandemic.

The annual gathering, which had been slated for May in Seattle, Washington, was **moved online** 3 June. In an ordinary year, *Spectrum's* reporters would fan out across the conference center and file at least 20 breaking news stories from the meeting; this year — with the help of you, our readers — we put together a roundup of the meeting's most exciting and important online presentations from home.

We are grateful to all who contributed their thoughts. Understandably, a fair number of you told us you were too busy with other duties — grant writing, homeschooling and caring for loved ones — to peruse the meeting's online offerings and 992-page abstract book.

But some of you found time to offer suggestions and thoughts, and to note some important trends: For instance, neuropsychology expert **Sven Bölte** of the Karolinska Institutet in Stockholm, Sweden, who was one of the meeting's keynote speakers, noticed a welcome uptick in the number of presentations from scientists working in underrepresented regions, including 31 from African researchers.

Let us know what you think. We will continually update this list with further suggestions.

With all good wishes,

The *Spectrum* team

GENES

The toll of copy number variation

Only a dozen **copy number variants** — DNA deletions and duplications — are associated with autism, yet many more shape a person's odds of having the condition. The model in this paper estimates the impact of deletions and duplications on intelligence and autism traits across more than 4,500 genes. Among the findings, the deleterious effect of deletions on intelligence quotient is three times greater than that of duplications; also, deletions and duplications take different tolls on social communication and behavior, but they affect motor skills equally.

Differential effects of deletions and duplications on autism risk across the genome

Upping the list of autism-linked genes

A new genomic analysis of more than 10,000 people with autism and nearly 20,000 of their first-degree relatives bumps the tally of genes associated with the condition from about 100 up to 161. Many of the new genes share functions with known autism-linked genes and are involved with RNA binding, transcriptional regulation and neuronal communication. The analysis also suggests that there is a higher inherited contribution to autism among families with multiple autistic members, compared with those that include only one autistic member.

Genomic analysis of 10,242 individuals with autism spectrum disorder (ASD) recruited online identifies 161 risk genes and new insights into the genetic architecture of multiplex families

Genetic phenotyping

By analyzing the sequences of roughly 200 autism candidate genes in more than 5,000 families in China with an autistic child, researchers have identified new genes that likely contribute to the condition. Some of the families carry inherited changes to genes previously linked to autism by way of spontaneous, or de novo, mutations; many parents in those families show traits of autism or other neurodevelopmental conditions. The findings suggest there are several genetic subtypes of autism linked to specific traits.

Autism high-risk genes and new genetic subtypes

The roots of resilience

Not everyone who harbors genetic mutations linked to autism shows autism traits. A new study begins to offer an explanation for this 'resilience.' Researchers analyzed DNA sequences from members of 1,201 families in which one child has autism. They found that about 8 percent of non-autistic parents and siblings carry mutations in established autism genes. What's more, resilient siblings tend to be girls and to have lower overall genetic '**risk scores**' for autism, suggesting that a mutation's effects depend partly on someone's sex and genetic background.

Differences in the genetic background contribute to risk and resilience to autism

TRAJECTORIES

Predicting adult outcomes

If clinicians could predict how children with autism might fare as adults, they could better tailor their support — but it's no easy task when working with a condition that has such variable outcomes. To

compare different forecasting tactics, researchers administered a battery of tests and questionnaires to 123 young adults referred for an autism diagnosis at age 2. They found that trait severity and intelligence quotient best predicted adult outcomes. The metric that best reflected the participants' subjective well-being — at least for more cognitively able adults — was tallying how many positive milestones, such as having steady employment and friendships, they had met.

Assessing longitudinal adult outcomes: A comparison of three approaches

Restricted and repetitive behaviors over time

A decrease in restricted and repetitive behaviors throughout childhood may forecast positive outcomes in adulthood, according to a study that followed 89 autistic individuals from age 2 to 25. Among autistic adults with an intelligence quotient of 70 or above, those who have at least one good friend, live independently and hold a steady job or attend college showed a significant decrease in verbal repetition and other so-called 'lower order' restricted and repetitive behaviors from age 9 to 18. Among autistic adults with an intelligence quotient below 70, a decrease from age 2 to 9 was linked to greater social contact or work outside of the home and daily living skills by age 25.

Adults with autism who achieve different functional outcomes show distinctive trajectories of RRBs from age 2 to 18

Sensory reactivity and communication abilities

Elementary-school-aged children on the spectrum who have sensory issues — sensory hypersensitivity, insensitivity or an unusual interest in sensory stimuli — tend to have poorer adaptive behavior skills later in life than do those without sensory issues. A new study partially extends these findings to infants and toddlers with autism. Among 90 autistic children, those who were most overreactive to sensory stimuli at 12 months of age had the lowest communication skills at 36 months, indicating a possible link between sensory issues and the development of language skills.

Sensory profiles as predictors of adaptive behavior in toddlers with autism

Developmental paths for white matter

White matter, the bundles of nerve fibers that connect brain regions, matures differently in autistic children, a new study confirms. The study involved 135 autistic children and 83 typical controls, who each underwent at least two brain scans from age 2 to 6 and a half years. The researchers found that before 30 to 36 months of age, autistic children's white matter tends to have more structural integrity than that of controls. By age 6 and a half, however, the opposite is true: Typical children have greater structural integrity than children with autism do.

A longitudinal diffusion weighted imaging study of white matter development in autism across early childhood

Shifts in severity

The severity of autism traits may change more than previously thought, according to a study that followed 169 autistic children from age 3 to 12. Past research has suggested that most children's

autism traits remain stable over time. By contrast, the new work shows that traits tend to wane from age 3 to 6 and increase from age 6 to 12, although the magnitude of those changes varies widely. Children whose traits diminish the most tend to be female and have a high intelligence quotient, superior daily-living skills and high levels of anxiety.

Autism symptom trajectories from early to middle childhood in the children of the Autism Phenome Project

Going through changes

Autistic children's cognitive and social abilities also shift over time, especially from age 2 to 13, a related study that tracked 90 participants suggests. The researchers divided children into three groups based on changes in their intelligence quotients (IQ) over time: The 'persistently low' group, which includes almost half of the children, started out with a below-average IQ that remained low; the 'persistently high' group, with about one-quarter of the participants, began the study with an above-average IQ and remained stable; the remaining children all belonged to the 'positive changers' group, and started out with a below-average IQ but had significant increases in that measure by adolescence. All three groups showed a decline in social motivation with age, and the 'persistently high' group showed an increase in signs of anxiety and depression. But the 'positive changers' showed gains in social awareness and functioning, suggesting a link between cognitive development and social skills.

Cognitive developmental trajectories, social functioning, and internalizing psychopathology in preadolescents with ASD

Coordinated actions

Some autistic children have problems with tasks that require coordinating their actions with those of a peer, a study has found. A group of 28 children with autism, aged 6 to 12, and another with 28 autistic adolescents completed two tests of coordinated joint actions: One required the participants to walk side by side with a peer while mirroring their companion's movements, and the other involved kicking and catching a virtual football. Adolescents tended to perform better than younger children on these tests; performance was best among those with a high IQ, superior fine and gross motor skills, and low levels of autism traits, suggesting that age, motor skills, autism trait severity and IQ contribute to a child's coordinated joint-action abilities.

Developmental trajectories in coordinated joint action and their link to motor functioning in ASD: Preliminary results

PREDICTIONS

From maternal to child health

A woman's health during pregnancy contributes to her child's overall health. So in this study, researchers analyzed medical records of the mothers of nearly 90,000 children in Israel to look at how various diagnoses in the year before conception and throughout pregnancy affect the odds of having a child with autism. The strongest associations, they found, included psychiatric, metabolic and genitourinary conditions.

The etiological relationships between maternal health and autism spectrum disorder

Early diagnosis

Early diagnosis is thought to lead to **improved outcomes** for autistic children, but to be diagnosed, children must be old enough to show autism traits — something that does not usually happen until around age 2. **Brain scans** might help doctors detect autism even earlier. In this preliminary study, researchers took two types of brain scans — looking at brain structure and how different brain areas communicate — in babies at 6 and 12 months of age and predicted with 80 percent accuracy which babies would be diagnosed at age 2. The researchers are working to replicate these results in a larger group of children.

The presymptomatic prediction of ASD using infant MRI

A research agenda for autism

Emily Simonoff, professor and head of child and adolescent psychiatry at Kings College London in the United Kingdom, outlined four key priorities for research on psychiatric conditions among autistic people in the coming decade. These include improving the accuracy of tools used to measure and assess mental health issues, developing more effective treatments for them, identifying their underlying mechanisms and building better models to predict who is most likely to have them.

Mental health in autistic people: Setting a research agenda for the coming decade

TRAITS

Pupil responses as a biomarker

A meta-analysis of 32 eye-tracking studies adds support to the idea that people with autism show distinct pupillary responses. Researchers found that, compared with controls, autistic individuals' pupils tend to be larger at rest and respond differently to stimuli — showing greater arousal in response to nonsocial stimuli than to social stimuli, for example. They also constrict less and more slowly in response to flashes of light. Regardless of whether pupillary responses can be validated as a **biomarker**, this work suggests that autism involves heightened arousal of the autonomic nervous system and atypical selective attention and information processing.

A meta-analysis of differences in pupillary measures between individuals with and without autism spectrum disorder

Heart health

Though autism is most often thought of as a neurodevelopmental condition, it affects other areas of the body, too, including the heart. To classify its cardiac impact, researchers are examining measures of heart health in 12 mouse models. So far, they've linked mutations in the autism genes **SHANK3**, **CHD8** and **ARID1B** to heart issues, such as alterations in heart rate, wall thickness in the left ventricle and the diameter of the aorta, with more data yet to be analyzed.

Cardiac comorbidities and their effect in autism spectrum disorder

Paying attention to gene variants

Children with mutations in a gene called **GRIN2B** often have autism, intellectual disability and attention problems. A new study points to a possible brain activity signature for attention problems in these children. Researchers used electroencephalography (EEG) to monitor brain activity in 7 children with GRIN2B mutations, 65 autistic children without mutations in the gene and 77 typical controls. They played a repeating sound and then measured the children's EEG response when the sound changed. Children with GRIN2B mutations had a larger EEG response to the new sound than did either typical or autistic children without GRIN2B mutations. This suggests that GRIN2B alters brain systems involved in controlling attention.

Connecting brain and behavior: Understanding GRIN2B disruptive mutations

Sensory subgroups

Most autistic people show atypical responses to sensory stimuli, but these responses can vary widely. To get a better handle on this diversity, researchers analyzed the sensory traits of 332 autistic children and adults, using a 38-item questionnaire filled out by parents. They found that the participants could be split into three groups — severe, moderate and low/mild — based on the frequency with which they show seven types of sensory behaviors. Those in the severe group tend to have the most problems with social and communication skills, whereas those in the moderate group tend to show the most signs of anxiety.

Dissecting the phenotypic heterogeneity in sensory behaviours in autism spectrum disorder: A factor mixture modelling approach

Measuring social communication

A widely used tool from the 1970s could serve as a simple and accurate way to assess social-communication skills among autistic children, a new study suggests. The tool, called the Clinical Global Impression – Severity (CGI-S) scale, is designed to measure the overall severity of psychiatric conditions, such as schizophrenia and bipolar disorder. It requires a clinician to rate a person's trait severity on a scale from 1 to 7, with lower scores indicating less impairment relative to other individuals with the same diagnosis. The scale has never been validated for use with autistic people, though, so researchers tested it with a group of 54 minimally verbal autistic children, who speak few or no words. Children with ratings on the CGI-S from 1 to 5 tend to initiate or respond to bids for joint attention more frequently than do their counterparts with ratings of 6 or 7. The two groups do not differ in the frequency of their restricted and repetitive behaviors, however, suggesting that the scale can accurately measure social communication skills among autistic children.

The Clinical Global Impressions-Severity (CGI-S) Scale: Measuring severity of social communication impairment among minimally verbal children with autism

TREATMENTS

Biases in play-based interventions

Play-based interventions are widely used to help children with autism develop social skills. This

systematic review of studies evaluating play therapies, however, questions whether they are effective. Researchers conducted a 'risk of bias' assessment on 76 studies of play therapies and found that 76 percent of them have flaws in their design and execution that could have skewed the results. The researchers highlight the need for improved study designs to evaluate these therapies.

Are play-based interventions for children with autisms spectrum disorder effective?

Stimulating the cerebellum

Jolting the **cerebellum** with a weak electrical current appears to improve performance on a social-learning task in adults with autism. Researchers used a technique called transcranial direct current stimulation to activate or inhibit cerebellar neurons in 10 adults with autism and 16 typical controls as they played a virtual ball-toss game. Without stimulation, the autistic participants showed less activity in the cerebellum, as measured by functional magnetic resonance imaging, during the task and less social learning than typical participants did. Delivering a current to activate cerebellar neurons impaired social learning in both groups, suggesting that the region helps with the acquisition of social information. A current that inactivated cerebellar neurons, however, improved social learning for the autistic participants.

The cerebellum modulates the acquisition of social information in autism

Oxytocin's effects

Daily doses of the hormone oxytocin, inhaled through the nose, do not improve sociability in children with autism, according to preliminary results from two new clinical trials. One of the trials, which lasted 24 weeks and was completed by 253 children with autism, found that the children who received oxytocin fared no better than those given placebo, according to a measure of social withdrawal and other tests of social function. The other trial spanned 12 weeks and involved nearly 54 autistic children. It similarly found that oxytocin has no effect on social withdrawal, but hints that the treatment may improve social recognition and ease emotional problems.

A large, heterogenous double-blinded trial of oxytocin to enhance social behaviours in ASD Randomized controlled trial of intranasal oxytocin in autism spectrum disorder

Anti-brain antibodies

Some mothers of autistic children have antibodies that attack a brain protein called CASPR2. In 2015, researchers showed that **injecting pregnant mice** with these antibodies can cause their pups to have autism-like traits. Now, the same group has created a new mouse model that better mimics how the antibodies occur in people. They coaxed pregnant mice to make their own antibodies against CASPR2 by injecting them with a piece of the CASPR2 protein. The mice's offspring show brain changes, repetitive behaviors and social difficulties, some of which the researchers were able to reverse by treating the mice with a drug that impairs brain cells called microglia.

Activation of microglia mediates ASD like phenotype in mice following in utero exposure to anti-CASPR2 antibodies

Shared learning

Autism specialists at 12 centers across North America have pilot-tested a videoconferencing program that allows them to share their expertise and clinical practices with one another — a program that has become even more valuable amid the current pandemic. Most participants reported high satisfaction with the program, which is called the Extension for Community Healthcare Outcomes (ECHO) model, and say that learning from other specialists led to changes in their own clinical practice. “This is an important program that is even more important now, given COVID-19,” says **Thomas Frazier**, professor of psychology at John Carroll University in University Heights, Ohio.

Novel approach to reducing variability in diagnostic and longitudinal care delivery through Echo Autism: Center Development & Support