

Autism Research Review

I N T E R N A T I O N A L

A quarterly publication of the Autism Research Institute—www.Autism.org

Reviewing biomedical and educational research in the field of autism and related disorders

Two studies explore possible effects of screen time on ASD or sensory problems in children

While some research suggests that there may be an association between greater use of screens and the development of autism spectrum disorders (ASD), a new meta-analysis reports no clear connection between the two. However, a second study suggests that early exposure to television or videos may be associated with an increase in atypical sensory behaviors.

In the first study, a meta-analysis by researchers in Israel and the United Kingdom, Yaakov Ophir and colleagues analyzed data from 46 studies with a total of 562,131 participants. The researchers did detect a small association between screen time and ASD, particularly in studies focusing on general screen use by children under 12 years of age. However, they say, “when accounting for publication bias [a form of bias that leads to more published studies supporting a hypothesis than disproving it], the findings were no longer statistically significant.”

The researchers also say their study could not rule out the possibility that any association between screen time and ASD works in the opposite direction—that is, that children with ASD may gravitate to screen time because they find screen activities less challenging than social interactions. They also cite research indicating that social media, educational television programs, and some video games can have positive effects for individuals with ASD.

The researchers conclude that “the findings of this systematic review and meta-analysis suggest that the proclaimed association between screen use and ASD is not sufficiently supported in the existing literature.”

In the second study, Karen Frankel Heffler and colleagues analyzed data collected between 2011 and 2014 on TV or DVD exposure of 1,471 toddlers at 12, 18, and 24 months of age. When the children were 33 months of age, the researchers used the Infant/Toddler Sensory Profile (ITSP), an assessment completed by parents or caregivers, to identify children with typical sensory processing as well as those with low registration (reduced sensitivity to stimuli), sensation-seeking behavior, sensory sensitivity, and/or sensation-avoiding behavior.

They report, “In this cohort study, early-life television or video exposure was associated with atypical sensory processing in low registration, sensation seeking, sensory sensitivity, and sensation avoiding domains of the ITSP, after controlling for perinatal and demographic variables.” However, they note, effects differed depending on the ages at which children were exposed. They conclude, “Further research is needed to understand why early media exposure is associated with specific sensory-related behaviors, including those seen in autism spectrum disorder, and if minimizing screen media at a young age can improve subsequent sensory-related outcomes.”

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“Screen time and autism spectrum disorder: a systematic review and meta-analysis,” Yaakov Ophir, Hananel Rosenberg, Refael Tikochinski,

Shani Dalyot, and Yuliya Lipshits-Braziler, *JAMA Network Open*, December 8, 2023 (free online). Address: Yaakov Ophir, Department of Education, Ariel University, 3 Kiryat Hamada St., Ariel 4070000, Israel, yaakovophir@gmail.com.

—and—
“Screen time may not be tied to autism spectrum disorder,” Lori Solomon, *Medical Xpress*, December 18, 2023.

—and—
“Early-life digital media experiences and development of atypical sensory processing,” Karen Frankel Heffler, Binod Acharya, Keshab Subedi, and David S. Bennett, *JAMA Pediatrics*, January 8, 2024 (online). Address: Karen Frankel Heffler, Department of Psychiatry, Drexel University College of Medicine, Philadelphia, Pennsylvania 19129.

—and—
“Exposure to TV may affect babies’ and toddlers’ ability to process the world around them, new study suggests,” news release, Drexel University, January 8, 2024.

ASD-associated gene variants may be under-identified by labs

Genetic variants associated with autism spectrum disorder (ASD) may often be missed by commercial laboratory tests, according to a new study.

Omri Bar and colleagues reanalyzed raw DNA sequencing data for 50 individuals with ASD who underwent, along with their parents, whole-genome sequencing (WGS) through an independent healthcare organization using a commercial laboratory. The researchers report, “Our study reveals that high-confidence diagnoses can be assigned to the majority (68%) of individuals with WGS followed by comprehensive reanalysis of raw sequence data.” In contrast, only 28% of cases were identified by WGS alone. The researchers add that half of the genetic variants associated with ASD that they detected were *de novo*—that is, they arose spontaneously, rather than being inherited.

Bar and colleagues conclude that “genetic laboratory reports...are insufficient for eliminating or identifying genetic causes of, and/or contributions to, ASD.” They add, “Since most clinicians are solely reliant on the report generated by genetic laboratories, the implications are that many patients and their families are being insufficiently counseled and genetically investigated con-

cerning important aspects of diagnoses and treatment of ASD.”

The researchers say, “Genetic data obtained were actionable in terms of altering management in the majority of cases. This figure does not include less-tangible benefits such as ending the diagnostic journey, avoiding additional unnecessary testing, and genetic counseling for potential recurrence risks.”

Commenting on the rapid rise in cases of ASD over the past few decades, the researchers note that the human genome changes only slowly over time and speculate that rates of *de novo* ASD-related gene variants “are accelerating due to some component in our rapidly, and profoundly, changing environment.” They add, “An alternative hypothesis is that [this] rate is relatively static over time, and these variants affect brain homeostasis, but disease may or may not develop dependent on the environment.”

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“Reanalysis of trio whole-genome sequencing data doubles the yield in autism spectrum disorder: *De novo* variants present in half,” Omri Bar, Elizabeth Vahey, Mark Mintz, Richard E. Frye, and Richard G. Boles, *International Journal of Molecular Sciences*, January 2024 (free online). Address: Richard Boles, *NeurAbilities Healthcare*, Voorhees, NJ 08043, rboles@neurabilities.com.

Multi-site study finds that pancreatic enzyme replacement therapy may aid children with ASD

A new multi-center study suggests that pancreatic enzyme replacement therapy may reduce behavior problems in young children with autism spectrum disorders (ASD).

Deborah Pearson and colleagues say research indicates that 65% of children with ASD have deficient levels of chymotrypsin enzyme activity. Chymotrypsin, an enzyme produced by the pancreas, helps to break down proteins into amino acids. A deficiency of chymotrypsin, the researchers say, can result in a lowered pool of essential amino acids including tryptophan (needed to produce serotonin) and phenylalanine (needed to produce dopamine). This, in turn, can affect behavioral and cognitive function.

To study the effects of supplementation with pancreatic enzymes, the researchers enrolled 190 children with ASD, all between three and six years of age, at 32 clinical sites around the United States. The first phase of the study was double-blinded and lasted for 12 weeks. In this phase, 92 of the children received the enzyme supplement in 900 mg doses sprinkled on their food three times a

day, while 98 received a placebo. In the second 24-week phase, which was nonblinded, all of the children took the supplement for 24 weeks.

In the first phase, compared to parents of children in the placebo group, parents of children in the treatment group reported that their children exhibited significantly less irritability, hyperactivity, noncompliance, and inappropriate speech. At the end of the 24-week phase, parents reported significant decreases in all of these behaviors as well as in lethargy and social withdrawal.

Pearson concludes, "This study demonstrated that pancreatic enzymatic replacement—which is thought to enhance the supply of essential amino acids necessary for the synthesis of neurotransmitters—was associated with improved behavioral function in preschoolers with ASD, with minimal side effects."

"Pancreatic replacement therapy for maladaptive behaviors in preschool children with autism spectrum disorder," Deborah A. Pearson, Robert L. Hendren, Matthew F. Heil, William R. McIntyre,

and Shane R. Raines, *JAMA Network Open*, November 30, 2023 (free online). Address: Deborah A. Pearson, Faillace Department of Psychiatry & Behavioral Sciences, McGovern Medical School, 1941 E Rd., Room 3.126 BBSB, Houston, TX 77054, deborah.a.pearson@uth.tmc.edu.

—and—

"Pancreatic enzymatic replacement therapy improves maladaptive behavior in preschool children with autism, finds study," news release, Halle Jones, University of Texas Health Science Center at Houston, December 18, 2023.

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Perivascular spaces, cerebral spinal fluid volume in infancy may play a role in ASD and sleep

The brain contains fluid-filled compartments called *perivascular spaces* that surround blood vessels and allow cerebral spinal fluid (CSF) to flush out neuroinflammatory chemicals and other waste. A new study suggests that infants with abnormally large perivascular spaces have a significantly elevated likelihood of developing autism spectrum disorders (ASD).

Dea Garic and colleagues, who conducted the study, collected data from three groups of infants:

- Forty-seven infants who had an elevated likelihood of developing ASD (due to having an older sibling with an ASD diagnosis) and who were diagnosed with ASD by the time they reached 24 months of age.
- One hundred and eighty infants with an elevated likelihood of developing ASD who did not receive an ASD diagnosis by 24 months of age.
- Eighty-four control infants who did not have an elevated likelihood of developing ASD and were not diagnosed with ASD by 24 months of age.

The researchers analyzed 870 magnetic resonance imaging (MRI) scans of the infants' brains to measure their perivascular space size and CSF volume at six, 12, and 24 months of age. They found that 30% of the infants who later developed ASD had

enlarged perivascular spaces by the time they were 12 months of age, and nearly half of the infants diagnosed with ASD had enlarged perivascular spaces by 24 months of age. Infants with elevated odds for ASD who had enlarged perivascular spaces at 24 months had a 2.2 times greater likelihood of being diagnosed with ASD compared to other children with elevated odds for ASD.

The researchers found that Infants with elevated odds for ASD who had enlarged perivascular spaces at 24 months of age had 2.2 times greater odds of developing ASD compared to other children with elevated odds for ASD.

"Our findings were striking, given that neuroradiologists typically view enlarged perivascular spaces as a sign of neurodegeneration in adults, but this study reported it in toddlers," Garic says. "This is an important aspect of brain development in the first years of life that should be monitored."

In addition, the researchers found that excess CSF volume at six months of age was associated with enlarged perivascular spaces at 24 months. This suggests, the researchers hypothesize, that impaired CSF circulation may lead to an accumulation of CSF and to enlarged perivascular spaces.

Because research suggests a link between enlarged perivascular spaces and sleep problems, Garic and colleagues ex-

amined data collected on a subset of the children approximately eight years after their initial evaluations. The results suggest, they say, that having enlarged perivascular spaces at 24 months of age "was associated with more frequent night disturbances regardless of familial likelihood or diagnosis of autism."

Garic comments, "Since autism is so highly linked with sleep problems, we were in this unique position to examine CSF dynamics and sleep. It was really striking to observe such a strong association separated by such a long period of time over childhood. But it really shows how perivascular spaces not only have an effect early in life, but they can have long-term effects, too."

"Enlarged perivascular spaces in infancy and autism diagnosis, cerebrospinal fluid volume, and later sleep problems," Dea Garic, Robert C. McKinstry, Joshua Rutsohn, Rebecca Slomowitz, Jason Wolff, Leigh C. MacIntyre, Leigh Anne H. Weisenfeld, Sun Hyung Kim, Juhi Pandey, Tanya St. John, Annette M. Estes, Robert T. Schultz, Heather C. Hazlett, Stephen R. Dager, Kelly N. Botteron, Martin Styner, Joseph Piven, and Mark D. Shen, *JAMA Network Open*, December 19, 2023 (free online). Address: Dea Garic, Carolina Institute for Developmental Disabilities, University of North Carolina at Chapel Hill School of Medicine, 101 Renee Lynne Ct, Carrboro, NC 27510, dea_garic@med.unc.edu.

—and—

"Enlarged spaces in infant brains linked to higher risk of autism, sleep problems," news release, Kendall Daniels, University of North Carolina at Chapel Hill School of Medicine, December 19, 2023.

EDITORIAL: Stephen M. Edelson, Ph.D.

Bernard Rimland's Impact: Sixty Years Since the Publication of *Infantile Autism*

In this milestone year of 2024, the Autism Research Institute commemorates the 60th anniversary of Dr. Bernard Rimland's groundbreaking work, *Infantile Autism: The Syndrome and Its Implications for a Neural Theory of Behavior*, published in 1964. While I have often referenced this seminal book in my editorials throughout the years, I believe it is important to take a moment to acknowledge not only the significance of the book itself but also its enduring impact on the broader landscape of autism research, understanding, and support.

Dr. Rimland's introduction to autism

When their son Mark was young, Bernard Rimland and his wife, Gloria, felt unsettled by the pediatrician's reassurance that he would outgrow the concerning behaviors he exhibited during infancy and early childhood. Mark displayed minimal eye contact, frequent tantrums, and repetitive behaviors such as rocking and finger flicking, and he seemed uninterested in interacting with his parents. While the pediatrician initially dismissed their concerns as typical parental worries, he advised them to monitor and document Mark's behaviors. Upon reviewing their observations, the pediatrician conceded that Mark's behavior was indeed unusual.

At this point, Gloria recalled encountering a description of an atypical child in a college textbook. After sifting through boxes, they located and read through the book, leading them to the realization that Mark exhibited characteristics consistent with autism.

Having just received a Ph.D. in experimental psychology, Rimland delved into research to find ways to assist his son. To his dismay, he discovered that the prevailing narrative within the professional community blamed autism on parents—particularly mothers, using the derogatory term “refrigerator mothers”—and alleged parental neglect without substantiating evidence.

Gloria once recounted a story to me about having dinner with a doctor and his wife, at which the atmosphere was more social than work-related. Toward the end of the evening, the doctor's wife made a surprising remark to Gloria: “I had expected you to be very distant and somewhat rude, but you're not.”

Similarly, many families with autistic children faced misunderstandings and criticisms from their social circles as well as from professionals. In 2003, PBS aired a

one-hour documentary titled *Refrigerator Mothers*, featuring mothers sharing their experiences of mistreatment and discrimination within their communities.

The genesis of *Infantile Autism*

Recognizing the lack of evidence for the parent-blaming perspective, Rimland countered by writing an article positing that the behaviors observed in children with autism indicated an underlying biological impairment, likely influenced by genetics, environmental factors, and neurology. Rimland had so much to say about the matter that the article expanded into a book over a five-year period.

The book garnered immediate international acclaim for Rimland's argument. Consequently, he was offered a one-year tenure at a think tank affiliated with Stanford University, during which he generated many ideas to address the challenges of autism. Among these was the establishment of a national parent network, facilitating the sharing of experiences among families, particularly regarding effective strategies for supporting their children. Rimland, alongside Ruth Sullivan, subsequently founded the National Society for Autistic Children, later renamed the Autism Society of America.

Parents' reactions to the book

Parents around the world rejoiced as the book gained recognition among professionals. They started reaching out to Rimland, who, despite his full-time job with the U.S. Navy, dedicated most of his evenings and weekends to responding to their inquiries and offering guidance. Over nearly five decades, he tirelessly communicated with parents through calls and letters while also advocating for researchers to explore ways to effectively support and care for individuals with autism.

Before Rimland's book, parents were often advised to seek marriage counseling while their children were enrolled in play



Bernard and Mark Rimland

therapy. However, once Rimland's argument gained traction, the healthcare community underwent a significant shift in approach. This led to the adoption of more aggressive measures, including the use of powerful medications such as Haldol and Mellaril, behavioral interventions (now recognized as Applied Behavior Analysis or ABA), and sensory integration therapy.

The relevance of Rimland's findings

Rimland's initial insights into autism remain relevant today. While some cases stem primarily from genetics, most clearly involve epigenetic factors. Additionally, many studies have reported various forms of co-occurring neurological impairment in individuals on the spectrum. In the 1990s, roughly 30 years after the publication of his book, Rimland underscored the link between autism, immune dysregulation, and gastrointestinal disease, a correlation that has since been validated. While numerous research studies over the last 60 years have examined various aspects of autism, Rimland pinpointed those closely associated with the fundamental foundations of autism.

During Rimland's last days, I spent much of my time visiting with him. He took great pleasure in reminiscing about writing his book and engaging in discussions about the book with parents and professionals. Since the ARI office had only a couple of copies of his books, I searched eBay for additional copies. In my searches, I came across a U.K. edition with a book cover, which was not included in the U.S. publication. I ordered it and presented it to Rimland as a gift. His reaction was one of speechless astonishment, as he had been unaware of the existence of the book cover. For those interested, you can see an image of the book cover along with a photo of Rimland taken around the time of the book's publication at www.Rimland1964Bookcover.com.



Gloria and Mark Rimland

Research Updates

Meta-analysis suggests association between prenatal exposure to cannabis and ASD or ADHD

A meta-analysis by researchers from Ethiopia and Australia suggests that prenatal exposure to cannabis may increase the odds of a child being diagnosed with an autism spectrum disorder (ASD) or attention-deficit/hyperactivity disorder (ADHD).

Abay Woday Tadesse and colleagues analyzed data from 14 studies, 10 on ADHD and four on ASD, with a total of more than 200,000 participants. They report, "In this systematic review and meta-analysis, we found that offspring exposed to prenatal cannabis use had an increased risk of ADHD symptoms and ASD compared with unexposed offspring. Adjustment for maternal mental health problems, maternal alcohol use, and tobacco smoking did not substantially alter the observed associations."

The researchers caution that larger studies are needed to confirm their results. However, they conclude, "The findings suggest the importance of implementing prevention and early interventions among offspring exposed to prenatal cannabis use."

"Prenatal cannabis use and the risk of attention deficit hyperactivity disorder and autism spectrum disorder in offspring: A systematic review and meta-analysis," Abay Woday Tadesse, Berihun Assefa Dachew, Getinet Ayano, Kim Betts, and Rosa Alati, *Journal of Psychiatric Research*, March 2024 (free online). Abay Woday Tadesse, School of Population Health, Curtin University, Kent Street, Bentley, WA, 6102, Australia, tadesse.woday@postgrad.curtin.edu.au.

Blood pressure drug may ease anxiety in children, young adults with ASD

Propranolol, a medication used to treat high blood pressure, may help to reduce symptoms of anxiety in children and young adults with autism spectrum disorders (ASD), according to a new study from the University of Missouri. Anxiety is a significant problem for many individuals with

ASD, affecting as many as 84% of individuals in this population.

David Beversdorf and colleagues enrolled 74 individuals, all between seven and 24 years of age, in a double-blind, randomized, placebo-controlled study. Participants were randomized to a 12-week course of propranolol or a placebo and were assessed at baseline and at six and 12 weeks. Sixty-nine of them completed the entire 12 weeks of the study.

The researchers say that while participants did not show any changes in social interaction or language, those taking the drug exhibited significantly less anxiety by the end of the study. Side effects were uncommon in study participants, although adverse effects of propranolol can include dizziness, fatigue, sleep problems, and congestion.

The researchers say that larger multicenter trials are needed to confirm their findings as well as to determine which individuals may be most likely to respond positively to the medication.

"Randomized controlled trial of propranolol on social communication and anxiety in children and young adults with autism spectrum disorder," David Q. Beversdorf, Bradley Ferguson, Samantha Hunter, Kathy Hirst, Bridget Lolli, Katherine R. Bellesheim, Amy U. Barton, Julie Muckerman, Nicole Takahashi, Kimberly Selders, Ryan Holem, Kristin Sohl, Peter Dyke, Janine Stichter, Micah Mazurek, and Stephen Kanne, *Psychopharmacology* (Berl.), December 13, 2023 (online). Address: David Beversdorf, Departments of Radiology, Neurology, and Psychological Sciences, University of Missouri, Columbia, MO 65211, beversdorfd@health.missouri.edu.

"Study shows blood pressure drug can reduce anxiety for people with autism," news release, University of Missouri, January 23, 2024.

Dealing with self-injurious behaviors?

Research points to numerous reasons for self-injurious behavior (SIB). ARI's free online tool assists professionals and parents in identifying potential treatments that may reduce or eliminate SIB. Responses to the survey questions may provide insight into one or more possible reasons why an individual engages in SIB. Links to published studies on causes and appropriate interventions are also offered based on each user's responses to survey questions.

www.Self-InjuriousBehavior.com

Photographs of the retina may aid in diagnosing ASD in children, adolescents

An artificial intelligence program designed to find patterns in photographs of the retina of the eye can identify children with autism spectrum disorders (ASD) with a high degree of accuracy, according to a new study from South Korea.

Jae Han Kim and colleagues used artificial intelligence to detect patterns in the retinas of children with ASD. They then tested their model on 958 children and adolescents between four and 19 years of age. Half of the children had ASD, and half were neurotypical.

The researchers report that their model identified every one of the autistic participants accurately and generated no false positives, although the model was less accurate at measuring the severity of autistic symptoms. They say their findings indicate that "retinal photographs may serve as an objective screening tool starting at least at age four years... which is earlier than the average age of 60.48 months at ASD diagnosis." However, they say it is unknown whether the technique will work for children younger than four years of age, as the retina is still developing in this group.

The researchers caution that their study had some limitations. For example, they did not control for medication use in participants, and they excluded children with co-existing conditions. However, they say, "Our findings suggest that the optic disc area is crucial for differentiating between individuals with ASD and [those with] typical development."

They conclude, "Although future studies are required to establish generalizability, our study represents a notable step toward developing objective screening tools for ASD, which may help address urgent issues such as the inaccessibility of specialized child psychiatry assessments due to limited resources."

"Development of deep ensembles to screen for autism and symptom severity using retinal photographs," Jae Han Kim, JaeSeong Hong, Hangyoung Choi, Hyun Goo Kang, Sangchul Yoon, Jung Yeon Hwang, Yu Rang Park, and Keun-Ah Cheon, *JAMA Network Open*, December 15, 2023 (free online). Address: Yu Rang Park, Department of Biomedical Systems Informatics, Yonsei University College of Medicine, Yonsei-ro 50-1, Seodaemun-gu, Seoul 03722, Republic of Korea, yurangpark@yuhs.ac.

"Using AI to diagnose autism in children," Bob Yirka, *Medical Xpress*, December 18, 2023.

Need help or information?

The Autism Research Institute maintains a toll-free calling center:
833-281-7165

Research Updates

Social anxiety disorder, ASD share strong association

There is a strong association between social anxiety disorder (SAD) and autism spectrum disorder (ASD) in adults, according to a new study by researchers in Italy.

Barbara Carpita and colleagues say, “Due to their similar behavioral presentation, it can sometimes be challenging to distinguish between SAD and the social avoidance that is frequently described in ASD. Moreover, a growing body of evidence is reporting that a significant proportion of subjects with ASD also meet the requirements for SAD and, vice versa, subjects with SAD tend to exhibit a higher prevalence of autistic traits.”

To explore possible links between SAD and ASD, the researchers analyzed data from assessments completed by 56 adults with a clinical diagnosis of SAD and 56 controls matched for age and gender. The assessments included the Social Anxiety Spectrum-Short Version (SHY-SV) and the Adult Autism Subthreshold Spectrum (AdAS Spectrum).

The researchers report that participants with SAD had significantly higher scores in all domains of both assessments as well as higher total scores compared to the controls. In addition, they say, SHY-SV total and domain scores correlated strongly and positively with all AdAS Spectrum domains and total score. They add, “AdAS Spectrum total score and Childhood/Adolescence, Non-Verbal Communication, Empathy and Restricted interests and Rumination domain scores were significant predictors of higher SHY-SV score.”

The researchers say their results confirm the link between SAD and autistic traits in adults, “describing not only high levels of autistic traits in SAD adults, but also significant correlations between many core features of the two disorders and a predictive role of autistic traits on higher SAD symptoms.”

“Presence and correlates of autistic traits among patients with social anxiety disorder,” Barbara Carpita, Benedetta Nardi, Chiara Bonelli, Enrico Massimetti, Giulia Amatori, Ivan Mirko Cremonese, Stefano Pini, and Liliana Dell’Osso, *Frontiers in Psychiatry*, Volume 14, December 2023 (online). Address: Barbara Carpita, Department of Clinical and Experimental Medicine, University of Pisa, Via Roma 67, Pisa 56127, Italy, barbara.carpita@unipi.it.

Did you know? The Autism Research Institute recently received its fifth annual four-star rating—the highest possible rating—from Charity Navigator.

More evidence seen of link between GI problems, ASD

A new large-scale study from China adds to evidence that intestinal problems may play a role in autism spectrum disorders (ASD).

In the study, Ting Yang and colleagues collected data from 1,222 children with ASD and 1,206 typically developing children from 13 cities in China. All of the children were between two and seven years of age.

The researchers evaluated the clinical symptoms of the children with ASD using the Childhood Autism Rating Scale (CARS), Social Responsiveness Scale (SRS), and Autism Behavior Checklist (ABC). They evaluated intestinal symptoms in both groups using the Gastrointestinal Severity Index (6-GSI).

The researchers report that rates of constipation, stool odor, and total intestinal symptoms were significantly higher in children with ASD than in controls. In addition, they say, “Autistic children presenting with intestinal comorbidity had significantly higher scores on the ABC, SRS, CARS, and multiple subscales than autistic children without intestinal symptoms, suggesting that intestinal comorbidity may exacerbate the core symptoms of ASD children.”

“Intestinal symptoms among children aged 2–7 years with autism spectrum disorder in 13 cities of China,” Ting Yang, Qian Zhang, Li Chen, Ying Dai, Fei-Yong Jia, Yan Hao, Ling Li, Jie Zhang, Li-Jie Wu, Xiao-Yan Ke, Ming-Ji Yi, Qi Hong, Jin-Jin Chen, Shuan-Feng Fang, Yi-Chao Wang, Qi Wang, Chun-Hua Jin, Jie Chen, and Ting-Yu Li, *Journal of Autism and Developmental Disorders*, December 7, 2023 (online). Address: Ting-Yu Li, Chongqing Key Laboratory of Childhood Nutrition and Health, Ministry of Education Key Laboratory of Child Development and Disorders, Department of Child Health Care, Children’s Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Chongqing, China, tyli@vip.sina.com.

Maternal contraception use may increase odds of ASD

The use of some forms of maternal birth control may slightly increase the odds of a child having an autism spectrum disorder (ASD), according to research from Denmark.

Marie Hargreave and colleagues analyzed data on more than one million Danish children born from 1998 through 2014. The researchers divided maternal birth control use into three categories: recent use (ending three months or less before pregnancy, or extending into pregnancy); previous use (ending more than three months before pregnancy); and no use.

Hargreave and her team calculated the association between maternal birth control use and ASD using incidence rate ratios (IRRs). IRRs are calculated by dividing the number of new cases in a time period by the number of individuals in the total group being studied.

The researchers report, “A slightly higher IRR was observed for maternal recent use of any hormonal contraception, compared to previous use.” This association, they say, was largely driven by non-oral progestin-only products. They add, “An increased IRR of infantile autism was also observed for recent use of the oral progestin-only products, compared to previous use.”

They conclude, “Our results suggest that maternal use of hormonal contraception may be associated with ASD risk in children, especially for the progestin-only products.”

“Maternal use of hormonal contraception and risk of childhood autism spectrum disorders: A Parental Exposures and Child Health (PECH) cohort study,” Marie Hargreave, Andrea H. Jezek, Caroline H. Hemmingsen, Elisabeth A.W. Andersen, Anne K. Pagsberg, Teresa Holmberg, Lina S. Mørch, and Susanne K. Kjaer, *Psychiatry Research*, Vol. 332, February 2024 (online). Address: Marie Hargreave, Virus, Lifestyle and Genes, Danish Cancer Institute, Copenhagen DK-2100, Denmark, mariehar@cancer.dk.

Visit the National Autism History Museum

To mark nearly a century of written history of autism, the Autism Research Institute (ARI) recently opened the National Autism History Museum—the first historical museum dedicated to autism. The four-room museum is located in the Kensington district in San Diego, California, adjacent to ARI’s main office.

Hours:

Monday-Thursday 10 a.m. to noon. or by appointment. To make an appointment, email us at NationalAutismHistoryMuseum@autism.org or call 833-281-7165.

Joint hypermobility more common in children and adolescents with autism

Joint hypermobility (a greater than normal range of movement in a single joint or group of joints) is significantly more common in children and adolescents with autism spectrum disorders (ASD) than in their neurotypical peers, according to a new study from Italy.

Domenico Marco Romeo and colleagues examined 67 children with non-syndromic ASD—in other words, ASD with no known cause—and 67 neurotypical controls. All of the children were between two and 18 years of age. The children were tested for hypermobility using an assessment called the Beighton scale or a variation of this tool. Children in the ASD group also underwent cognitive, verbal, and behavioral assessments.

The researchers report, “This study found a higher rate of joint hypermobility in both ASD preschool age (63%) and school age children (73%) than those reported in the literature for typically developing children using the Beighton score at the same age (less than 10%).” In addition, the children in the ASD group had significantly higher joint hypermobility scores than the neurotypical children participating in the study. However, joint hypermobility did not correlate with cognitive skills or severity of ASD.

The researchers conclude, “The results of our study suggest that joint hypermobility could be considered as a clinical characteristic of ASD patients. Therefore, joint hypermobility needs to be assessed in all ASD children in order to schedule a better rehabilitation program and to allow for the possibility of applying the research in practice.”

“Relationship and new prospectives in joint hypermobility in children with autism spectrum disorder: preliminary data,” Domenico Marco Romeo, Marianna Moro, Mariangela Pezone, Ilaria Venezia, Federica Mirra, Margherita De Biase, Agnese Polo, Ida Turrini, Maria Rosaria Lala, Chiara Velli, Francesca Sini, Domenico Dragone, Eugenio Mercuri, and Claudia Brogna, *Journal of Personalized Medicine*, December 18, 2023 (free online). Address: Claudia Brogna, claudia.brogna@policlinicogemelli.it.

Ketogenic diet may reduce seizures by changing microbiome

More than a century ago, physicians at Johns Hopkins University discovered that a strict ketogenic diet—very high in fat, moderate in protein, and very low in carbohydrates—could reduce seizures in a sizable percentage of children with treatment-refractory epilepsy (a problem for a significant number of children with autism). Now, scientists at the University of California at Los Angeles report that the diet may work by altering the gut microbiome in ways that protect against seizures.

Gregory Lum and colleagues collected stool samples from 10 children with refractory epilepsy both before and one month after the children began a clinical ketogenic diet. They then transplanted the children’s microflora into the guts of germ-free mice.

The researchers found that the mice that received the post-treatment microflora were more resistant to induced seizures than the mice that received the pre-treatment microflora. Both the mice and the children also exhibited metabolic changes related to energy production, amino acid metabolism, and oxidation of fatty acids. The metabolic changes persisted in the mice even when the animals ate a standard diet, suggesting, the researchers say, that “the source microbes

are maintained under non-ketogenic dietary conditions.” In addition, the mice exhibited changes in the activity of certain genes linked to epilepsy.

While around 30% of children on the clinical ketogenic diet become seizure-free, and around 60% experience a significant reduction in seizures, the diet (which is stricter than most popular “keto” diets) is difficult to follow and has side effects including nausea, constipation, and fatigue. The researchers hope that by identifying the specific changes caused by the ketogenic diet, it may be possible to make the diet more effective or to come up with other treatments that mimic its beneficial effects.

“Ketogenic diet therapy for pediatric epilepsy is associated with alterations in the human gut microbiome that confer seizure resistance in mice,” Gregory R. Lum, Sung Min Ha, Christine A. Olson, Montgomery Blencowe, Jorge Paramo, Beck Reyes, Joyce H. Matsumoto, Xia Yang, and Elaine Y. Hsiao, *Cell Reports*, December 26, 2023 (free online). Address: Gregory Lum, glum@g.ucla.edu, or Elaine Hsiao, ehsiao@g.ucla.edu.

“The keto diet protects against epileptic seizures, and scientists are uncovering why,” news release, Kelsie Sandoval, University of California, Los Angeles, December 18, 2023.

Life-long care needs impact family members’ quality of life

Parents and other relatives often provide life-long support for adults with autism spectrum disorders (ASD), and a new study from Germany suggests that this support impacts the family members’ mental and physical health.

Sophia Dücker and colleagues note, “Family caregivers of autistic adults represent a highly underrecognized population in clinical research, healthcare, society, and policy.” To assess these caregivers’ mental and physical quality of life, the researchers surveyed 149 family members providing support to adults with ASD. In addition to providing sociodemographic information, participants completed assessments related to caregiving and health-related quality of life.

The researchers report, “Family caregivers of autistic adults reported significantly

lower physical and mental health-related quality of life compared to the general population.” In particular, higher subjective caregiver burden (a measure of the demands, challenges, and stressors experienced by caregivers) and greater severity of the care recipient’s ASD correlated with poorer mental quality of life.

The researchers also note that “compared to family caregivers of patients with severe mental illness or Down syndrome, participants in the current study reported the lowest mental health-related quality of life scores.”

They conclude, “Healthcare providers working with autistic adults and their families should be aware of the potential impairment of caregivers’ health status and form a routine to assess and monitor caregivers’ health-related quality of life, for example as part of the intake assessment or in primary care.”

“Health-related quality of life in family caregivers of autistic adults,” Sophia Dücker, Sabine Bart, Petia Gewohn, Hannah König, Daniel Schöttle, Alexander Konnopka, Pascal Rahlff, Frank Erik, Kai Vogeley, Holger Schulz, Nicole David, and Judith Peth, *Frontiers in Psychiatry*, December 18, 2023 (free online). Address: Sophia Dücker, Department of Medical Psychology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany s.duecker@uke.de.

—www.Autism.Jobs—

**A Free Resource for Job Seekers, Caregivers, Job Coaches,
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At this site, you can discover the advantages of hiring individuals with autism, access practical information designed to help candidates with autism become “job ready,” and learn how to create autism-friendly workplaces.

Chronic constipation in young children associated with higher rate of ASD

Researchers in Japan and the United States report that children with chronic functional constipation (CFC)—in other words, chronic constipation due to unknown causes—have an elevated rate of autism spectrum disorders (ASD).

Fumiaki Akama and colleagues analyzed data on 55 young children. Thirty of the participants had CFC, while 25 were controls who did not suffer from constipation. To evaluate the children's psychiatric symptoms, the researchers asked their caregivers to fill out the Child Behavior Checklist (CBCL) and Aberrant Behavior Checklist-Japanese version (ABC-J). A child psychiatrist also evaluated the children for ASD.

The researchers report, "The mean Aberrant Behavior Checklist score and frequency of individuals with autism spectrum disorder were significantly higher in the chronic functional constipation group. After adjusting for age and sex, chronic functional constipation was significantly associated with autism spectrum disorder." In addition, they say, "In the chronic functional constipation group, the frequency of onset was significantly higher in children with autism spectrum disorder under one year of age. When treated, the mean duration of constipation was significantly longer in children with autism spectrum disorder."

The researchers conclude, "In this study population, children with CFC had a high frequency of ASD and children with ASD had a longer duration of CFC and experienced CFC earlier in life." They comment, "If clinicians encounter children with CFC and behavioral problems, they should consider the possibility of ASD as a comorbidity. When children with CFC develop ASD, pediatricians, pediatric surgeons, and child psychiatrists should work closely together to treat both CF and ASD effectively and immediately."

"Psychiatric features of children with chronic functional constipation: focusing on individuals with autism spectrum disorder," Fumiaki Akama, Katsunaka Mikami, Yasushi Orihashi, Syunya Takase, Kyuta Hanawa, Keita Nishikawa, Nat-suru Watanabe, Keitaro Kimoto, Yuki Takahashi, Yuichi Onishi, Juan Salas, Kenji Yamamoto, and Shigeru Ueno, *Journal of Autism and Developmental Disorders*, January 24, 2024 (free online). Address: Katsunaka Mikami, Department of Psychiatry, Tokai University School of Medicine, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan, achapaou@is.icc.u-tokai.ac.jp.

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Atypical reflex may help to identify nonverbal kids with ASD

Measuring the way in which children's eyes move when they turn their heads may help to identify those with autism spectrum disorders, according to a new study by researchers at the University of California at San Francisco.

Chenyu Wang and colleagues initially studied mice with a variant of a gene called SCN2A that is associated with severe autism. The researchers tested the vestibulo-ocular reflex (VOR) of the mice, a reflex that keeps images stabilized on the retina when the head moves by producing eye movements opposite to the motion of the head. The researchers discovered that mice with the gene variant had an unusually sensitive VOR.

Next, the researchers asked five children with SCN2A-linked autism and eleven of their neurotypical siblings to participate in an experiment in which the children were rotated to the left and right in a chair while their eye movements were tracked. The researchers found that the children with autism, but not their neurotypical siblings, exhibited a hypersensitive VOR. This hypersensitivity, they say, could help to explain the very strong reactions to sensory stimuli exhibited by many children with ASD.

The researchers say that if their findings are confirmed, measuring VOR could help clinicians diagnose children with ASD earli-

er. Study coauthor Kevin Bender comments, "We can measure it in kids with autism who are nonverbal or can't or don't want to follow instructions. This could be a game-changer in both the clinic and the lab."

"Impaired cerebellar plasticity hypersensitizes sensory reflexes in SCN2A-associated ASD," Chenyu Wang, Kimberly D. Derderian, Elizabeth Hamada, Xujia Zhou, Andrew D. Nelson, Henry Kyoung, Nadav Ahituv, Guy Bouvier, and Kevin J. Bender, *Neuron*, February 26, 2024 (online). Address: Kevin Bender, kevin.bender@ucsf.edu.

—and—
"A simple eye reflex test may be able to assess autism in children," Medical Xpress, February 28, 2024.

Are you an adult with autism?

Increasing numbers of adults are being diagnosed with autism spectrum disorders (ASD). To learn more about the symptoms of autism in adults, see ARI's article at:

<https://autism.org/autism-symptoms-and-diagnosis-in-adults/>

At this site, you will also find a listing of free webinars for adults with autism.

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AUTISM AND SLEEP—RESEARCH UPDATES

Dara S. Manoach, Ph.D.

—May 15, 2024—

1 p.m. Eastern time

CHANGES IN AUTISM SYMPTOMS ACROSS CHILDHOOD

Einat Waizbard-Bartov, Ph.D.

—May 29, 2024—

1 p.m. Eastern time

BLOOD-BRAIN BARRIER DYSFUNCTION IN PEDIATRIC ACUTE NEUROPSYCHIATRIC SYNDROME (PANS) AND REGULATION

Noor A. Hussein, Ph.D. and Ayan Mondal, Ph.D.

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