

Autism Research Review

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

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

Anticholinergic drugs may raise dementia risk in adults with ASD and intellectual disabilities

Adults with autism spectrum disorder (ASD) and intellectual disability who take high doses of anticholinergic (AC) medications may be at elevated risk for cognitive decline, according to a new study.

AC drugs, used to treat a wide range of medical problems, inhibit the action of the neurotransmitter acetylcholine. Long-term use of these drugs is associated with de-

Noting that individuals with ASD and intellectual disability are at elevated risk for dementia, the researchers say, “AC medication use may represent a potential modifiable risk factor for decrements in cognition in autistic adults with higher support needs.”

clines in cognition in elderly individuals, particularly in those taking larger doses. In a 2024 study specific to autism, Goldie McQuaid and colleagues found that middle-aged and older adults with ASD who took higher amounts of AC medications reported experiencing an elevated rate of memory problems and cognitive decline. Participants in that study did not have intellectual disability.

No link seen between male circumcision and autism

Neonatal male circumcision (NMC) does not increase the likelihood of a later autism spectrum disorder (ASD) diagnosis, according to U.S. researchers.

Two observational studies, one in 2013 and another in 2015, suggested a potential link between NMC and ASD, leading to speculation that the pain of circumcision or the administration of acetaminophen during the procedure could be responsible. To investigate this question further, Monica McGrath and colleagues analyzed data collected on 2,771 boys at 14 sites around the United States. Of this cohort, 66% were circumcised within a month after birth, and 7%

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In their new research, McQuaid and her team studied autistic adults with legally authorized representatives, in order to focus on individuals with both ASD and intellectual disability. Analyzing data on 512 individuals between 18 and 68 years of age, they report, “The majority (66.41%) of autistic adults were taking at least one AC medication and 31% were taking clinically-meaningful levels of these medications.” After controlling for age and birth sex, the researchers found that “greater potency of AC medications was associated with both caregiver-reported memory challenges and behavioral/cognitive changes associated with cognitive decline.”

Noting that individuals with ASD and intellectual disability are at elevated risk for dementia, the researchers say, “AC medication use may represent a potential modi-

fiable risk factor for decrements in cognition in autistic adults with higher support needs.” They recommend that clinicians evaluate the medication regimens of individuals with ASD and intellectual disability to determine the potential impact of AC drugs on cognition. “Further,” they say, “it may be appropriate to begin such evaluations earlier in the lifespan, given the potential for earlier and thus more prolonged exposure to potent AC medications in this population.”

“Characterization of anticholinergic medication use and its associations with everyday memory problems and cognitive decline in autistic adults with higher support needs,” Goldie A. McQuaid, Nancy Raitano Lee, and Gregory L. Wallace, *Autism Research*, August 13, 2026 (free online). Address: Goldie McQuaid, gmcquaid@gmu.edu.

Autism increase due largely to rising diagnoses in females

Rates of diagnosed autism spectrum disorder (ASD) in males remained steady over the past decade while ASD diagnoses of females climbed, according to a study by U.S. researchers.

Erick Messias and colleagues analyzed electronic health record data collected on more than 171,000 children, adolescents and adults between 2016 and 2024, determining the annual incidence of newly recorded diagnoses of ASD (including Asperger syndrome). They report that while the overall incidence of new ASD diagnoses rose among children and adolescents—particularly in the period following the COVID pandemic—“this aggregate growth masked a significant sex disparity.” They note, “Among adolescents and adults, incidence rates for females increased significantly or trended upward, whereas rates for males remained stable or declined.” In addition, the researchers found that females received diagnoses an average of 3.4 years later than males.

The researchers say their findings suggest that “the reported increases in first ASD diagnoses post-pandemic are due to increased

recognition of females with autism spectrum disorder rather than a uniform population level increase.”

They add, “For clinicians, these data underscore the necessity of adapting screening practices to detect the subtler presentations of ASD in females and ensuring that diagnostic capacity extends beyond early childhood into adolescence and adulthood. The delay of 3.4 years in diagnosis for women has concrete consequences: later access to support, accommodations, and community connection during formative developmental periods.” The researchers add that future studies should explore whether delays in the diagnosis of ASD in females stem from inadequate screening tools, practitioner knowledge gaps, or other factors.

“Autism spectrum disorder incidence by age and sex in a U.S. health care system, 2016 to 2024,” Erick Messias, Emily Casanova, Regina Huang, Siri Battula, Rachel Loftin, McKenna Walsh, and Ping-I Lin, *JAMA Network Open*, July 22, 2026 (free online). Address: McKenna Walsh, St. Louis University School of Medicine, 1402 S. Grand Blvd., St. Louis, MO 63104, mckenna.walsh@health.slu.edu.

Study questions whether PDA is a valid diagnosis

A meta-analysis by researchers in Australia casts doubt on whether pathological demand avoidance (PDA) is a legitimate diagnosis.

Many of the symptoms of PDA, which was first described in the 1980s, are also symptoms of autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder, and/or oppositional defiant disorder. Features include passivity during infancy, a strong resistance to ordinary life demands, social impairments, volatile moods, language delays, an interest in role-playing, obsessive behaviors, clumsiness, and physical awkwardness.

Dylan Company and Joe Anthony Rotella note that PDA “remains a contentious diagnosis with several interpretations and no validated diagnostic criteria.” Currently, PDA is not formally recognized as a diagnosis by the Diagnostic and Statistical Manual of Mental Disorders or the International Classification of Diseases. Some researchers argue that it is a subtype within the autism spectrum, while others believe it is a distinct condition.

To investigate the issue, the researchers analyzed data from 12 studies on PDA. Nine of the studies involved children, two involved adults, and one involved both age groups. Most of the studies relied on surveys or self-reported questionnaires, while several used diagnostic tools.

The researchers found that all of the studies appeared to be at high risk for methodological bias because of their design and the means by which they recruited participants. “There was considerable inconsistency in the way PDA was identified across studies,” they say, “with a large proportion of studies relying on subjective rather than objective measures.” Moreover, they say, the diagnostic tools used to identify PDA in some studies have not been validated for this purpose.

The researchers suggest that the studies they reviewed may suffer from circular logic, a logical fallacy in which the premise of an argument assumes the conclusion to be true—“in other words,” they say, “the diagnostic test identified PDA in this person because the person who underwent the diagnostic test has PDA.” They conclude that this “makes it difficult to support any of the diagnostic tools pertaining to PDA, let alone the condition itself.”

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“A systematic review of pathological demand avoidance (PDA): a veritable diagnosis or a case of circular logic?”, Dylan Company and Joe Anthony Rotella, *Journal of Autism and Developmental Disorders*, July 2026 (free online). Address: Joe Anthony Rotella, joe.a.rotella@nh.org.au.

No link seen between circumcision, ASD (continued from page 1)

had an autism diagnosis based on parental report of a clinician diagnosis or validated assessments.

The researchers report, “Among 1,840 circumcised males, 108 (6%) had autism, compared with 84 of 931 uncircumcised males (9%).” After adjusting for other factors, they found no correlation between circumcision and ASD. Acetaminophen use was uncommon in the neonatal period, they add, “further suggesting that an acetaminophen-mediated pathway linking NMC to ASD is unlikely.”

“These findings,” they say, may provide reassurance for families considering NMC and those who have already elected to have NMC for their child.”

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“Neonatal medical male circumcision and

child autism diagnosis,” Monica McGrath, Xiuhong Li, Lisa P. Jacobson, Bennett Leventhal, Judy L. Aschner, Brennan Baker, Karla Cardoso Garcia, Aisha S. Dickerson, Amy J. Elliott, Jody Ganiban, Amanda Goodrich, Daniel B. Horton, Melinda Jarnecke, Sarah Keim, Brian K. Lee, Courtney D. Lynch, Mark Klebanoff, Abdul-Manaf Mutaru, Ruby H. N. Nguyen, Rebecca J. Schmidt, Hyeong-Moo Shin, Lauren C. Shuffrey, Jonathan L. Slaughter, Annemarie Stroustrup, Zhaozhong Zhu, Aaron A. R. Tobian, and M. Kate Grabowski, for the ECHO Cohort Consortium, *JAMA Pediatrics*, August 3, 2026. Address: Monica McGrath, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe St., Baltimore, MD 21205, mmcgrat4@jhu.edu.

—and—

“Study: Male circumcision just after birth does not increase autism risk,” news release, Johns Hopkins Bloomberg School of Public Health, August 4, 2026.

Is the prevalence of Phelan-McDermid higher than thought?

The prevalence of Phelan-McDermid syndrome (PMS) may be much higher than previously estimated, according to researchers in the United States and Australia.

PMS, a genetic condition caused by a deletion or mutation of the SHANK3 gene, causes a wide range of medical, cognitive, and behavioral problems, and the majority of people with the condition have autism spectrum disorders (ASD). SHANK3 deletions or mutations are believed to cause up to 1% of cases of ASD.

To determine the prevalence of PMD in the United States, Tess Levy and colleagues analyzed data from nearly 180,000 individuals with ASD who underwent genetic testing. The researchers combined data from 10 sources including clinical genetic testing laboratories, academic medical centers, and autism research programs.

The researchers found that the prevalence of PMD in the United States is 13.7 cases per 100,000 births, far higher than earlier estimates of 2.5 to 10 cases per million births. This suggests, they say, that “more than 45,000 individuals in the United States are currently living with PMS, assuming an average lifespan.”

Levy comments, “The large gap between known and estimated cases is likely due in large part to the fact that many individuals with developmental disabilities and autism are never offered genetic testing. Families may also face insurance barriers or may receive tests that do not adequately evaluate the SHANK3 gene.”

The low rates of genetic testing are especially concerning, the researchers say, because “genetic diagnoses are becoming increasingly actionable.” They note, “Be-

yond providing families with a better understanding of their child’s condition and future trajectory, a genetic diagnosis may qualify individuals for clinical trials or targeted therapies that could significantly alter outcomes.”

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“Prevalence of Phelan-McDermid syndrome estimated to be ~1:7300 using a multisource model,” Tess Levy, David Lapidus, Kate Friedman, Paige Siper, Larry Glass, Liza Squires, Mary Hames, Joseph D. Buxbaum, Genetic Testing Consortium, and Alexander Kolevzon, *Autism Research*, July 2026 (free online). Address: Alexander Kolevzon, alexander.kolevzon@mssm.edu.

—and—

“Autism research finds Phelan-McDermid syndrome may affect 1 in 7,300 people: More common than previously thought,” news release, Mount Sinai Hospital, July 10, 2026.

Quotable...

“Taken together, [multiple] studies suggest that many childhood psychiatric presentations may simply convey common consequential behavioral pathways. Children can display similar outward symptoms despite profoundly different underlying etiologies. The future of pediatric psychiatry may depend less on refining symptom labels and more on identifying what lies beneath them.”

—Elena S. Monarch and Piero Pavone, in “Editorial: Severe mental illnesses in children: unravelling developmental trajectories, neuropsychiatric impairments, and chronic pain,” *Frontiers in Child and Adolescent Psychiatry*, July 20, 2026

EDITORIAL

Autism beyond the brain: the overlooked role of connective tissue

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For decades, autism research and clinical care have understandably focused on the brain and behavior. Yet autistic people and their families have long reported something that does not fit neatly within that framework: high rates of chronic pain, gastrointestinal problems, fatigue, sleep disturbance, autonomic symptoms, and other complex physical health concerns.

Increasingly, research suggests that connective tissue may be one important piece of this puzzle.

Ehlers-Danlos syndromes (EDS) are heritable connective tissue disorders, while hypermobility spectrum disorders (HSD) describe symptomatic joint hypermobility that does not meet criteria for EDS. Hypermobility EDS (hEDS), the most common form of EDS, and HSD can involve much more than flexible joints. People may experience joint instability and injury, chronic pain, profound fatigue, gastrointestinal problems, dysautonomia, sleep difficulties, and immune-related symptoms, among other health concerns. Strikingly, many of these same problems occur disproportionately in autistic people.

The association between autism and hypermobility-related conditions is no longer based simply on anecdotal reports. A nationwide Swedish study found that people diagnosed with EDS were more than seven times as likely to have an autism diagnosis as matched controls (Cederlöf et al., 2016). Studies approaching the question from the opposite direction have found a similar pattern. In one large study of autistic adults, 28% had generalized joint hypermobility, compared with only 11% of non-autistic adults. Symptomatic hypermobility showed an even stronger association with autism. But an especially important finding from this study receives less attention: *Asymptomatic hypermobility was also significantly associated with autism* (Glans et al., 2022).

This suggests that we may need to think beyond EDS and HSD diagnoses alone. Instead, there may be a broader spectrum of connective tissue variation enriched within the autistic population. For some people, that variation may amount to little more than unusually flexible joints.

For others, it may be accompanied by pain, instability, fatigue, or the multisystem features that characterize HSD or hEDS.

Why does this matter?

Many of the health conditions associated with EDS/HSD can profoundly affect quality of life. Cardiovascular involvement can include mitral valve prolapse and aortic root dilation, both of which are recognized features of hEDS (Rashed et al., 2022). Connective tissue differences may also affect the mechanical properties of blood vessels. Increased vascular compliance has been proposed as one factor contributing to blood pooling and orthostatic intolerance (a form of dysautonomia) in EDS/HSD, although the mechanisms underlying this relationship are still being investigated (Miller et al., 2020; Roma et al., 2018).

Physical health must become a more central part of how we think about autistic quality of life. For families struggling with pain, fatigue, dizziness, gastrointestinal problems, sleep disruption, and declining physical function, understanding the biology behind these problems is not an academic exercise. Recognition can lead to appropriate evaluation, better symptom management, and, potentially, a very different quality of life.

Dysautonomia, including orthostatic intolerance and postural orthostatic tachycardia syndrome (POTS), can cause dizziness, rapid heart rate, anxiety-like symptoms, weakness, brain fog, exercise intolerance, and debilitating fatigue. Heightened activation of the sympathetic, or “fight-or-flight,” nervous system can also produce feelings of internal agitation and anxiety and may heighten sensitivity to sensory input. For an autistic person already prone to sensory overload, this additional physiological stress may intensify feelings of overwhelm and potentially contribute to shutdowns or meltdowns. What appears to be worsening anxiety or autistic distress may therefore sometimes be influenced by an underlying physical stressor.

Chronic musculoskeletal pain can interfere with sleep, concentration, mobility, school, employment, and everyday activities. Gastrointestinal dysregulation and immune abnormalities, including mast cell-related disorders, are also frequently reported in hypermobility-related populations (Casanova et al., 2020).

Importantly, these conditions do not merely appear on two separate lists of “au-

tism comorbidities” and “EDS comorbidities.” There is emerging evidence that the relationships may be interconnected. Researchers have found that joint hypermobility statistically mediates part of the relationship between neurodivergence and both orthostatic intolerance and musculoskeletal pain (Csecs et al., 2022). More recent research in people with chronic pain and fatigue has produced similar findings (Quadt et al., 2026).

We do not yet know why autism and connective tissue differences overlap. One possibility is shared genetics. Genes do not necessarily perform a single job in a single organ: The same gene may play important roles in both brain development and the cells that produce and maintain connective tissue. Genetic variation affecting such a gene could therefore have effects on both neurodevelopment and connective tissue. Other possibilities include shared developmental pathways and immune-related mechanisms. These possibilities are increasingly being studied, but we do not yet know which mechanisms—or combination of mechanisms—account for the association. But uncertainty about mechanism should not become an excuse for overlooking what we already know clinically.

An autistic child with chronic leg pain, frequent joint injuries, fatigue, gastrointestinal problems, or dizziness when standing should not automatically have these difficulties attributed to autism, anxiety, behavior, or deconditioning. Even changes in anxiety, sensory tolerance, or episodes of shutdown or meltdown may warrant asking whether an underlying physical problem is contributing. Likewise, an autistic adult whose physical health progressively limits work, exercise, self-care, or family participation deserves investigation of those symptoms on their own merits.

This does *not* mean that every autistic person has EDS, or that every flexible autistic person needs a medical diagnosis. Rather, autism should increase clinicians’ awareness of the possibility of generalized joint hypermobility and related physical health problems. Asking a few additional questions about joint instability, chronic pain, fatigue, orthostatic symptoms, gastrointestinal problems, and family history could identify people who warrant further evaluation.

Research must broaden its perspective as well. We need large, carefully characterized studies that examine connective tissue traits across the autism spectrum—not only people who already carry an EDS or

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Research Updates

Online ABA found effective

Applied Behavior Analysis (ABA) services delivered entirely online may be a valid alternative to traditional in-person therapy for many children with autism spectrum disorders (ASD), according to a study by U.S. researchers.

In traditional ABA, a highly trained individual—typically a Board Certified Behavior Analyst (BCBA)—oversees therapists who provide services in family homes. Study authors William Edwards and Brittany Wierzbza note that this intensive, in-person therapy can create challenges for families who struggle to afford the cost of the therapy, have scheduling issues, or live in an area with a shortage of therapists. In addition, they say, the high turnover of in-home therapists can hinder children's progress.

To see if a telehealth approach might be a viable alternative, the researchers conducted a retrospective analysis of data collected on 504 children who received focused online ABA therapy delivered by a BCBA for an average of 2.6 hours per week. All services were provided by the BCBA, including assessment, direct therapy, therapy protocol modification, and caregiver training. The researchers evaluated changes in the children based on a battery of tests administered every six months, analyzing data only for children who underwent a baseline assessment and at least one follow-up assessment.

The researchers found that children receiving services delivered entirely online showed improvements in adaptive skills, behavior outcomes, and family quality of life. In addition, they say, 95.1% of families reported that the services they received were effective.

Wierzbza comments, "Autism therapy is under immense pressure. Families, providers and payors all need more flexible options to meet rising demand with fewer BCBAs. This study shows that virtual therapy, when led by

BCBAs, can effectively bridge that gap to produce meaningful progress, avoid escalations in care, and support a stable quality of life for families."

"Fully virtual, focused Applied Behavior Analysis services: acceptability and feasibility study," William H. Edwards and Brittany C. Wierzbza, *JMIR Publications*, June 10, 2026 (free online). Address: William H. Edwards, Center for Behavior Analysis, Clemson University, B-111 Barre Hall, Clemson, SC 29634, wedwar2@clemson.edu.

—and—

"Families report positive outcomes from fully virtual, BCBA-delivered, focused autism support program," news release, *JMIR publications*, July 8, 2026.

Daytime naps may reduce behavior problems

Researchers in the United Kingdom report that daytime naps may help to reduce behavior problems in autistic children who have trouble sleeping at night.

Yiqing Zhong and Dagmara Dimitriou investigated the associations between sleep and behavior in 53 Chinese children between six and 12 years of age. (The researchers studied children in China because daytime naps for schoolchildren are routine there.) Of the children, 26 were autistic and 27 were neurotypical. The researchers measured the children's sleep habits using actigraphy (which measures movements), sleep diaries, and the Children's Sleep Habits Questionnaire.

They report, "Autistic children showed significantly more sleep disturbances than neurotypical peers, including greater bedtime resistance, longer sleep onset delay, more frequent night waking, and shorter total sleep. Night waking was a key correlate of behavioral problems in both groups." However, they say, "Longer nap durations were associated with weaker associations between sleep disturbances and behavioral difficulties, reducing aggression in autistic children and internalizing symptoms in typically developing children."

The researchers say a short nighttime sleep tended to result in a longer nap the next day. However longer naps during the day did not affect the following sleep that night.

They conclude, "These findings suggest that culturally embedded nap routines may serve as a low-cost, context-sensitive strategy to support behavioral functioning in neurodivergent populations."

"Unlocking the potential of habitual napping to moderate the association between sleep distur-

bances and behavioral problems among autistic and typically developing children," Yiqing Zhong and Dagmara Dimitriou, *Autism Research*, April 2026. Address: Dagmara Dimitriou, Sleep Education and Research Laboratory, Department of Psychology and Human Development, University College London-Institute of Education, London, UK WC1H 0AL, d.dimitriou@ucl.ac.uk.

Prenatal exposure to heavy metals may raise likelihood of a child having ASD

Prenatal exposure to heavy metals may increase the likelihood of a child having an autism spectrum disorder (ASD), according to U.S. researchers.

Pi-I Debby Lin and colleagues analyzed 479 blood samples and 482 urine samples from pregnant women to determine if prenatal exposure to heavy metals affected their children's scores on the Social Responsiveness Scale-Second Edition (SRS-2)—a measure of traits associated with ASD—or the odds of the children having ASD. They report, "Analyses of individual metals revealed that maternal blood lead and mercury levels were associated with increased autism-related traits, whereas urinary metals showed no meaningful associations. Additionally, we observed a significant association between maternal blood cadmium levels and an ASD diagnosis in children."

Testing combinations of metals, the researchers found that higher maternal blood levels of arsenic, cadmium, mercury, and lead were associated with elevated SRS-2 scores on social awareness and cognition. Some differences in vulnerability to heavy metals were seen between males and females, which the researchers say "suggest[s] potential sex differences in susceptibility to metal-related neurodevelopmental effects."

They conclude, "These results highlight the importance of reducing harmful metal exposures during pregnancy and considering combined exposures and sex-specific effects when evaluating risks to early brain development."

"Associations of prenatal metal exposures with autism-related outcomes in the ECHO cohort," Pi-I Debby Lin, Andres Cardenas, Kristen Lyall, Deborah Bilder, Debra A. Mackenzie, Sara Nozadi, Brandon J. Rennie, Rebecca Schmidt, Heather Volk, Aisha S. Dickerson, and Emily Okena, *Environmental Epidemiology*, July 2026 (free online). Address: Pi-I Debby Lin, Division of Chronic Disease Research Across the Lifecourse, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, 401 Park Dr., Suite 401, East Boston, MA 02215, p_lin@hphci.harvard.edu.

Visit the National Autism History Museum

The National Autism History Museum is the first historical museum dedicated to autism. The museum is located in San Diego, California.

Hours:

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

www.NationalAutismHistoryMuseum.com

Research Updates

Restrictive eating may up risk for rickets in children

The restrictive eating habits of many children and teens with autism spectrum disorders (ASD) put them at increased risk for rickets due to vitamin D deficiency, according to a study by researchers in the United States. Rickets can cause bone softening and deformities, delayed growth, muscle weakness, delayed motor skills, and pain in the lower body.

Mohamed Said and colleagues performed a retrospective chart review at a children's hospital to identify patients with ASD who exhibited symptoms of nutritional rickets. They included all patients who had clinical findings indicative of rickets, laboratory evidence of vitamin D deficiency with or without low calcium levels (a side effect of vitamin D deficiency), and radiographic findings consistent with rickets. They also collected information on where the children lived, their symptoms, their dietary patterns, their clinical examination findings, the results of laboratory and imaging tests, and their case management and outcomes.

The researchers identified 11 patients with rickets, ranging from four to 16 years of age. All of them resided in low-income neighborhoods. All had extremely low vitamin D levels, eight had very low serum calcium (leading to seizures in three children), and seven had musculoskeletal problems.

Most of the children improved with nutritional treatment alone. However, significant complications included bilateral fractures of the femur and deformities severe enough to require surgery.

The researchers comment, "Older children and adolescents with ASD and highly selective diets, particularly those living in very low-opportunity neighborhoods, may develop severe nutritional rickets with presentations ranging from subtle gait changes and progressive valgus deformity ["knock knees" or related bone and joint misalignments] to hypocalcemic seizures. Orthopedists should maintain a high index of suspicion for metabolic bone disease in this population and obtain a focused dietary history, targeted laboratory testing, and radiographs to enable timely treatment and prevent morbidity."

The new research follows previous studies linking restrictive eating habits to an increased risk for beriberi, due to vitamin B1 deficiency; scurvy, due to low vitamin C levels (see ARRI Vol. 37, No. 1); and blind-

ness, due to low vitamin A levels (see ARRI Vol. 38, No. 4).

"Orthopaedist beware: severe nutritional rickets and autism spectrum disorder," Mohamed Said, Alexandra Falkenberg, Leila Alvandi, Edina Gjonbalaj, Alexa J. Karkenny, and Melinda S. Sharkey, *Journal of the Pediatric Orthopaedic Society of North America*, August 2026 (free online). Address: Melinda Sharkey, Montefiore Einstein Department of Orthopedic Surgery, 3400 Bainbridge Ave., Bronx, NY 10467, msharkey@montefiore.org.

Fertility challenges linked to slight rise in children's neurodevelopmental issues

Researchers in the United States report that fertility challenges may be associated with a slight increase in neurodevelopmental problems in children.

Linda Kahn and colleagues examined data collected on 15,382 mother-child pairs at 44 sites across the U.S. and Puerto Rico. Using survey data and medical records, they identified parents with a history of infertility diagnoses, in vitro fertilization (IVF) or other fertility treatments, multiple miscarriages, and/or long periods of inability to conceive. They also assessed the children's development between two and 10 years of age, using parent questionnaires and clinician diagnoses of autism spectrum disorder (ASD) or attention-deficit/hyperactivity disorder (ADHD).

The researchers found that children of parents with fertility challenges exhibited slightly more behavior problems, slightly more ASD-like traits, and increased odds of an ASD diagnosis, even when the children were conceived without fertility treatment. They also found that non-IVF fertility treatments were associated with higher odds of ADHD. However, there was no clear association between in vitro fertilization and neurodevelopmental outcomes.

The researchers say, "Our results support the growing consensus that the elevated risk of adverse neurodevelopmental outcomes among children conceived via infertility treatment derives from underlying pathology, not the treatment itself." They add, "Non-IVF treatment was associated with ADHD, warranting further research into specific indications for treatment that may increase risk of offspring neurodevelopmental problems."

"Subfecundity, infertility treatment, and child neurodevelopment," Linda G. Kahn, Alison E.

Hipwell, Joseph B. Stanford, Noya Galai, Haozuo Zhao, Akram N. Alshawabkeh, Judy L. Aschner, Emily S. Barrett, Ricardo P. Bertolla, Kim Nail Cajachagua Torres, Carlos A. Camargo, Jr., Jose F. Cordero, Lisa A. Croen, Sean C. Deoni, Sema Gogcu, Julie B. Herbstman, Margaret R. Karagas, Kaja Z. LeWinn, Kristen Lyall, Cynthia T. McEvoy, Kimberlee McKay, Thomas G. O'Connor, J. Richard Pilsner, Susan L. Schantz, Rebecca J. Schmidt, Alicia K. Smith, Greta N. Wilkening, E. Zhang, Yeyi Zhu, Akhgar Ghassabian, and the ECHO Cohort Consortium, *JAMA Network Open*, June 8, 2026 (free online). Address: Linda G. Kahn, New York University Grossman School of Medicine, 227 E. 30th St., Room 607, New York, NY 10016, linda.kahn@nyulangone.org.

—and—

"Fertility challenges associated with small differences in children's neurodevelopment, NIH study finds," news release, June 9, 2026.

CHD may elevate odds of children having autism

Children with congenital heart disease (CHD) may have a significantly elevated likelihood of having an autism spectrum disorder (ASD), according to a study by researchers in the United States and Singapore.

Nuria Lisset Ontiveros Perez and colleagues analyzed data on 94 children with CHD who required surgery before their discharge from a neonatal ICU and who underwent a high-risk infant follow-up between 18 and 30 months of age. The researchers identified children who received a positive score on the Modified Checklist for Autism-Revised/Follow-Up (M-CHAT-R/F) at their follow-up visit. In addition, they identified children who subsequently received an ASD diagnosis.

They report, "[T]he prevalence of autism likelihood based on screening results and the prevalence of the diagnosis of autism was more than three times those rates within the general population." They also found that the M-CHAT-R/F had an acceptable overall accuracy in distinguishing between children with and without autism.

They conclude, "These results support reliable and routine autism screening for children with CHD at 18-30 months of age and prompt diagnostic evaluations for those with positive screen results."

"Autism screening and diagnosis in children with congenital heart disease," Nuria Lisset Ontiveros Perez, Pamela M. Rios, Virginia A. Marchman, Ramkumar Aishworiya, Stella Firth Wang, and Heidi M. Feldman, *Frontiers in Pediatrics*, June 16, 2026 (free online). Address: Heidi M. Feldman, hfeldman@stanford.edu.

Autistic adults with social anxiety may find CBT with stressor exposure helpful

Autistic adults with social anxiety may benefit significantly from a modified CBT (cognitive behavioral therapy) intervention that includes controlled exposure to a social stressor, according to researchers in Australia.

Bruna Roisenberg and colleagues enrolled 32 adults with autism spectrum disorders (ASD) and social anxiety into an eight-week CBT program tailored specifically for individuals with autism. CBT is a popular approach for treating social anxiety, and one key CBT strategy involves controlled exposure to situations that provoke anxiety. However, the researchers note that little is known about the effectiveness of controlled exposure for individuals with ASD.

In the sixth week of the intervention, the researchers asked participants to give a short speech on an anxiety-provoking topic (for example, how social anxiety had affected their lives) in front of their group members and therapists. Participants completed questionnaires before and after the speeches, assessing how anxious they felt, how well they thought they did, and how they thought the members of the audience saw them.

The researchers say, “Most participants felt less anxious after the speech than they expected, showing that the task helped reduce fear.” They also found that “reductions in fear during the speech task were meaningfully related to broader symptom change, predicting a significant degree of symptom improvement from pre- to post-therapy.” Analysis showed that the responses of participants with ASD to the social exposure task were similar to those seen in non-autistic individuals with social anxiety disorder.

Roisenberg and colleagues conclude, “These results show that with the right support, autistic adults can benefit from public speaking tasks and that therapy should be tailored to their unique experiences and strengths.”

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“Exposure, extinction, and cognitive appraisals in autistic adults with social anxiety: evidence from a structured speech exposure task,” Brunna B. Roisenberg, Kelsie A. Boulton, Emma E. Thomas, Dorothy Yu, and Adam J. Guastella, *Autism Research*, June 2026 (free online). Address: Adam J. Guastella, Clinic for Autism and Neurodevelopment (CAN) Research, Brain and Mind Centre, Children’s Hospital Westmead Clinical School, Faculty of Medicine and Health, University of Sydney, Sydney, Australia, adam.guastella@sydney.edu.au.

Anxiety common in adults with ASD, may increase over time

Anxiety is common in adults with autism, and researchers in the United Kingdom report that it may worsen over time.

Aphrodite Eshetu and colleagues analyzed data collected from 5,270 adults between 50 and 91 years of age. They followed participants for eight years, annually assessing their autistic traits and general anxiety symptoms.

“A trait-based approach offers a valuable alternative to diagnosis-based recruitment,” the researchers say, “particularly in midlife and older populations where autism is frequently under-recognized or misdiagnosed. This approach allows researchers to identify people with elevated autistic traits and characteristics who may not have received a formal diagnosis, thus capturing a broader and potentially more representative sample of autistic adults.”

Using a method called growth mixture modeling, the researchers identified three distinct groups. The first group, comprising more than 85 percent of participants, had very low levels of anxiety that remained stable over the course of the study. The second group, around 12 percent of participants, had slightly higher but still low levels of anxiety that stayed stable over time. The third group, comprising two percent of participants, experienced anxiety that increased

over the course of the study, from mild to clinically significant levels.

The researchers found that adults with high autistic traits were more than four times more likely than other participants to develop clinically significant anxiety over time. They were also twice as likely to experience persistent low-level anxiety.

The researchers say factors that could cause increasing anxiety as people with autistic traits age include social isolation, greater exposure to stress or trauma, and barriers to health care. They comment, “Given the detrimental consequences of chronic anxiety for physical and mental health, these findings highlight the need for increased, tailored support for adults on the autism spectrum.”

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“The association between autistic traits and trajectories of anxiety in middle-aged and older adults: an 8-year growth mixture model analysis,” Aphrodite Eshetu, Saloni Ghai, Anne Corbett, Clive Ballard, Adam Hampshire, Elizabeth O’Nions, William Mandy, Joshua Stott, Amber John, and Gavin R. Stewart, *Nature Mental Health*, June 1, 2026 (free online). Address: Joshua Stott, j.stott@ucl.ac.uk, or Gavin Stewart, gavin.stewart@kcl.ac.uk.

—and—
“Middle-aged and older adults with autistic traits face rising anxiety over time, study finds,” news release, Kings College London, June 1, 2026.

Urine test may aid in spotting children at high odds for ASD

A simple urine test may be able to identify children at high likelihood for autism spectrum disorder (ASD), according to researchers in the United States and United Kingdom.

Christina Flynn and colleagues measured the concentrations of microbial metabolites—molecules produced by microorganisms in the gut—in 52 children diagnosed with ASD and 47 neurotypical children. The children were between two and 11 years of age, and lived in four different areas across the United States.

The researchers found that nearly all children with ASD had at least one metabolite level exceeding the highest level observed in controls, and some levels were 100 to 1,000 times higher than in controls. Overall, they say, “Twenty-three of 24 microbially derived metabolites were statistically significantly higher in ASD than in typically developing participants.” Metabolites found in elevated levels included a number that are involved in the serotonin, dopamine, or melatonin pathways or have a connection with yeast activity.

The researchers say their urine test correctly identified 90 percent of the children with ASD, and did not incorrectly identify

any neurotypical children as autistic. Based on their results, they propose a new subtype of ASD they call “ASD associated with microbially-derived metabolites,” or ASD-MDM.

If future research confirms the urine test’s efficacy, the researchers say, it could aid in early diagnosis and help lead to the development of treatment strategies aimed at establishing a healthy microbiome.

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“Elevated microbially-derived metabolites in autism: a possible diagnostic screening test for a distinct ASD phenotype,” Christina K. Flynn, Kevin Carr, Paul Whiteley, Khemlal Nirmalkar, Andrew Bellinghiere, Juergen Hahn, Hongbin Liu, Halil Arici, Laura Hewitson, Morgan Devlin, Elena L. Pollard, Khyatiben V. Pathak, Krystine Garcia Mansfield, Anakaren Rosales Torres, Patrick Pirrotte, Daniel B. Kalb, Rebekah Keen, Victoria Kenyon, Alessio Fasano, Rosa Krajmalnik-Brown, James B. Adams, and Sarah Kadzielski, *Molecular Psychiatry*, May 26, 2026 (free online). Address: James Adams, Biodesign Center for Health Through Microbiomes, Arizona State University, Tempe, AZ, 85287, jim.adams@asu.edu.

—and—
“New urine test may spot autism risk in children ages two to 11, study finds,” news release, Sandy Keaton Leander, Arizona State University, May 27, 2026.

Study suggests that some cases of autism spectrum disorder may involve copper deficiency

Researchers in Japan report evidence that copper deficiency may play a role in autism spectrum disorders (ASD).

Noriyoshi Usui and colleagues measured 21 elements in the plasma of 112 people with ASD and 115 neurotypical controls and detected a significant association between lower plasma copper levels and higher scores on clinical measures of ASD symptoms. Brain MRI scans also showed that participants with ASD had reduced white matter volume, which was associated with social symptoms.

The researchers note that white matter is composed largely of nerve fibers wrapped in insulating myelin, which is produced by a type of glial cell called oligodendrocytes. Their findings suggest, they say, that low levels of copper could affect the way in which glial cells support brain circuit development.

To test this idea, the researchers created a mouse model of developmental copper deficiency. The copper-deficient mice exhibited altered social behavior and repetitive behaviors. Copper deficiency also reduced oligodendrocyte-lineage cells in the brain,

impaired these cells' maturation, and decreased myelin formation.

The researchers were able to identify a molecular pathway connecting copper deficiency to the brain changes seen in the mice. They found that copper deficiency disrupted regulation of blood vessel formation and metabolic responses in the developing brain, leading to oxidative stress, mitochondrial dysfunction, and altered mitophagy (removal of damaged mitochondria). These changes, in turn, led to suppressed mTOR signaling. The mTOR pathway is a cellular signaling pathway that plays crucial roles in cell growth, metabolism, and oligodendrocyte development. Activating mTOR signaling in the copper-deficient mice restored oligodendrocyte maturation and improved social behavior.

The researchers comment, "To our knowledge, this is the first study to mechanistically link copper deficiency to ASD-related glial and behavioral phenotypes using an integrative human-animal model approach." Their findings, they say, offer insight into how systemic metal imbalances can contribute to

ASD by disrupting trace element-dependent neurodevelopmental processes.

They stress, however, that their findings do not indicate that individuals with ASD should be taking copper supplements, noting that the population with ASD is diverse and copper deficiency may play a role in only a subgroup of individuals.

"Copper deficiency impairs oligodendrocyte maturation and social behavior via mitophagy and mTOR suppression in ASD," Noriyoshi Usui, Miyuki Doi, Stefano Berto, Kiwamu Matsuoka, Rio Ishida, Hana Miyauchi, Yuuki Fujiwara, Koichiro Irie, Michihiro Toritsuka, Takahira Yamauchi, Takaharu Hirai, Min-Jue Xie, Yoshinori Kayashima, Naoko Umeda, Keiko Iwata, Kazuki Okumura, Taeko Harada, Taiichi Katayama, Masatsugu Tsujii, Hideo Matsuzaki, Manabu Makinodan, and Shoichi Shimada, *Science Advances*, April 2026 (free online). Address: Noriyoshi Usui, Department of Developmental Neuroscience, Graduate School of Medical and Dental Sciences, Niigata University, Niigata 951-8510, Japan, noriyoshi.usui.med@niigata-u.ac.jp.

—and—

"Copper imbalance tied to autism's social symptoms and white matter development," news release, Niigata University, June 2, 2026.

Free Webinars

ARI offers free webinars for caregivers, professionals, and individuals with autism. Free Certificates of Participation are available upon passing an online quiz for most webinars. Some events offer Continuing Education Units and/or Continuing Medical Education credits. Upcoming webinars include:

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DECODING FACE PROCESSING IN AUTISM

Jason W. Griffin, PhD

—December 2, 2026—

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You can sign up for webinars or view previous webinars at <https://autism.org/webinars>. Space is limited—watch your email, or visit us on Facebook and X for updates and registration links.

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Autism beyond the brain: the overlooked role of connective tissue (continued from page 3)

HSD diagnosis. We need to understand why some hypermobile autistic people remain relatively asymptomatic while others develop chronic pain, dysautonomia, immune problems, and substantial disability. And we need to investigate the biological pathways that may connect neurodevelopment, connective tissue, autonomic regulation, and immune function.

Most importantly, physical health must become a more central part of how we think about autistic quality of life. For families struggling with pain, fatigue, dizziness, gastrointestinal problems, sleep disruption, and declining physical function, understanding the biology behind these problems is not an academic exercise. Recognition can lead to appropriate evaluation, better symptom management, and, potentially, a very different quality of life.

True, autism involves the brain. But autistic people live in bodies. Our research—and our healthcare—must give those bodies the attention they deserve.

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