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Autism Research Review

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

Two new meta-analyses cast doubt on link between acetaminophen and autism, other NDDs

While some researchers have reported a possible association between prenatal exposure to acetaminophen (Tylenol/paracetamol) and autism, two separate multinational research groups have detected no clear link.

In the first study, Jameela Sheikh and colleagues conducted an "umbrella" review of nine reviews, including a total of 40 observational studies, that explored acetaminophen use during pregnancy and children's odds of developing autism spectrum disorders (ASD) or attention-deficit/hyperactivity disorder (ADHD). Four of the reviews they examined included meta-analyses of multiple studies.

The researchers say, "The reviews reported a possible to strong association between maternal paracetamol intake and autism or ADHD or both in offspring." However, they say, "Seven of the nine reviews advised caution when interpreting the findings owing to the potential risk of bias and confounding in the included studies." They add that confidence in the quality of the reviews (based on AMSTAR 2, which measures the quality of studies) was "low to critically low."

In two studies that adjusted for familial factors, the researchers say, the association between ASD or ADHD disappeared when sibling-controlled analyses were performed. The researchers say, "This disappearance of association in the sibling analyses, previously observed in the whole cohort, suggests that shared family factors, such as parental mental health, genetic predisposition, and socioenvironmental background, explain much of the observed risk."

They conclude, "Existing evidence does not clearly link maternal paracetamol use during pregnancy with autism or ADHD in offspring."

In the second paper, Anick Bérard and colleagues reviewed 16 studies exploring prenatal acetaminophen exposure and the odds of neurodevelopmental disorders (NDDs) in children. They report, "Acetaminophen use during pregnancy was not associated with a statistically significant increased risk of ASD when considering physician-based diagnoses." While they detected a modest increase in ADHD in children exposed to acetaminophen *in utero*, they say this was most likely due to inherent study biases and underlying genetic factors.No clear association was seen between prenatal acetaminophen exposure and other NDDs.

Emphasizing that most current studies exhibit significant methodological weaknesses, both research groups call for carefully designed studies that account for factors such as familial and genetic influences, the reasons for acetaminophen use, and the duration, dosage, and timing of use.

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"Maternal paracetamol (acetaminophen) use during pregnancy and risk of autism spectrum disorder and attention deficit/hyperactivity disorder in offspring: umbrella review of systematic reviews," Jameela Sheikh, John Allotey, Soha Sobhy, Maria Nieves Plana, Hilario Martinez-Barros, Harshitha Naidu, Fatima Junaid, Reecha Sofat, Ben W. Mol, Louise C. Kenny, Melissa Gladstone, Helena Teede, Javier Zamora, and Shakila Thangaratinam, *British Medical Journal*, November 2025. Address: Shakila Thangaratinam, s.thangaratinam@liverpool.ac.uk.

—and—

"Tylenol during pregnancy: No strong evidence ties use to autism or ADHD risk," news release, *British Medical Journal*, November 6, 2025.

—and—

"Systematic review and meta-analysis: acetaminophen use during pregnancy and the risk of neurodevelopmental disorders in childhood," Anick Bérard, Judith Cottin, Lisiane F. Leal, Cyndie Picot, Justine Pleau, Jan M. Friedman, Per Damkier, Michel Cucherat, Sura Alwan, Lucie Jurek, Louise M. Winn, Bruce C. Carleton, Andréa D. Bertoldi, Sonia M. Grandi, Reem Masarwa, Philippe Dodin, Michael Ceulemans, Robert W. Platt, Mikail Nourredine, Erika Björkström Gram, Areti Angeliki Veroniki, Jérôme Massardier, and Andrea C. Tricco, *Journal of the American Academy of Child & Adolescent Psychiatry*, November 2025 (free online). Address: Anick Bérard, 3175 Chem. de la Côte-Sainte-Catherine, Montréal, QC H3T 1C5, Canada, anick.berard@umontreal.

—and—

"Review finds no link between acetaminophen use in pregnancy and neurodevelopmental disorders," news release, Elsevier, November 9, 2025.

(See related ARRI position statement on page 7 of this issue.)

Researchers report more evidence linking ASD, GI problems

A study by U.S. researchers adds to evidence that children with autism spectrum disorders (ASD) are more likely than neurotypical children to experience persistent gastrointestinal problems.

Bibiana Restrepo and colleagues analyzed data collected on 322 children with ASD and 153 neurotypical controls. The children had been evaluated at up to three time points when they were between two and 12 years of age.

The researchers report, "Children with autism presented with more gastrointestinal symptoms at each time point, and they were also more likely to experience multiple and persistent gastrointestinal symptoms." Nearly half of the children in the ASD group experienced gastrointestinal symptoms at one time point, 40% experienced symptoms at two time points, and 30% experienced symptoms at all three time points. The most commonly reported symptoms were constipation, diarrhea, gas, bloating, and abdominal pain.

In addition, the researchers say, "The presence and number of gastrointestinal symptoms were associated with greater impairment in internalizing behaviors, sleep, communication, sensory processing, and repetitive behaviors."

The researchers urge clinicians to ask about gastrointestinal issues during routine checkups for patients with ASD. In addition, they say, "[W]hen parents raise concerns about a new behavior problem arising, it is important to screen for gastrointestinal symptoms, as children with autism may not be able to report their symptoms at all and parent observation is the most important source of information."

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"A longitudinal evaluation of gastrointestinal symptoms in children with autism spectrum

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Exposure to specific airborne pollution components may increase likelihood of ASD diagnosis

Prenatal and early-life exposure to specific components of fine-particulate airborne pollutants may increase the likelihood of a child developing an autism spectrum disorder (ASD), according to researchers in Canada and the United States.

Previous research has suggested a link between fine particulate matter with a diameter of 2.5 micrometers or less ($PM_{2.5}$) and neurodevelopmental disorders including ASD. In the new study, Maxime Cloutier and colleagues examined the effects of exposure to specific components of $PM_{2.5}$ during different stages of prenatal and early-life development.

The population-based retrospective study examined data from more than two million children, including nearly 20,000 with an ASD diagnosis. Exposures were calculated based on maternal postal codes at the time of delivery, using satellite data, chemical transport models, and ground-based measurements.

The researchers say, "In this large population-based cohort from Ontario, Canada, we observed significant associations between prenatal $PM_{2.5}$ exposure, particularly its components SO_4^{2-} [sulfate] and NH_4^+ [ammonium], and increased ASD risk in children. The effect size of this association was largest during the second and third trimesters, suggesting critical windows of vulnerability. Additionally, O_3 [ozone] exposure in late pregnancy and the first postnatal year was significantly associated with ASD."

The researchers say the effects of pollutants were greater for male than female children, with only sulfate showing a significant association with ASD in female children. They also detected larger effects of $PM_{2.5}$ in urban settings, and in low- and middle-income neighborhoods.

They conclude, "These findings underscore the potential importance of early-life environmental exposures and reinforce the need for public health strategies to reduce air pollution, particularly in urban and socioeconomically disadvantaged communities."

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"Prenatal exposure to fine particulate matter components and autism risk in childhood," Maxime Cloutier, Chengchun Yu, Robert Talarico, Steven Hawken, Hong Chen, Scott Weichenthal, Sabit Cakmak, Christopher Hebbern, Anna Gunz, Aaron van Donkelaar, Randall V. Martin, Jean-Nicolas Côté, and Éric Lavigne, *JAMA Network Open*, October 23, 2025. Address: Éric Lavigne, Health Canada, 269 Laurier Ave W, Ottawa, Ontario, Canada, K1A 0K9, eric.lavigne@hc-sc.gc.ca.

—and—

"Prenatal exposure to specific fine particles linked to autism risk," news release, Justin Jackson, Medical Xpress, November 3, 2025.

See related editorial on page 3.

individuals with ASD show greater generosity toward strangers

A study by researchers in Germany and the United Kingdom supports earlier findings that compared to neurotypical individuals, individuals with autism spectrum disorders (ASD) exhibit more generosity toward people who are socially distant from them.

Paul AG Forbes and colleagues note, "Previous work suggests autistic individuals show a flatter decline in generosity towards socially distant others compared with non-autistic participants. We investigated whether this enhanced prosociality towards socially distant others in autism was driven by genuinely higher prosociality or instead a preference for repetitive responding."

The researchers asked 37 individuals with ASD and 38 non-autistic individuals to participate in their study. Participants filled out the Social Value Orientation questionnaire, which asks participants how they would share money with other people at six different degrees of closeness (for instance, a best friend, an acquaintance, or a stranger).

"Compared with non-autistic participants," the researchers report, "autistic participants were more generous to people they did not feel close to." This difference, they say, was not due to repetitive responding or to any differences in attitudes about money.

The researchers note that their findings are consistent with those of two previous studies. They suggest that the generosity to strangers exhibited by participants with ASD may reflect a more consistent implementation of fairness norms by autistic individuals. "This is supported," they say, "by the finding that autistic individuals make more consistent decisions, are more inflexible when following moral rules, and are more likely to endorse fairness as a foundational principle for their moral outlook."

They conclude, "Our findings support an emerging view that while autistic people often face challenges navigating their social worlds, autism is associated with more prosocial behavior."

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"Increased prosocial value orientation in autistic adults," Paul AG Forbes, Gillian Hughes, Leonhard Schilbach, Sarah White, and Tobias Kalenscher, *Autism*, October 28, 2025 (free online). Address: Paul AG Forbes, Comparative Psychology, Institute of Experimental Psychology, Heinrich-Heine University Düsseldorf, Universitätsstraße 1, 40225 Düsseldorf, Germany, paul.forbes@hhu.de.

Visit the National Autism History Museum

To mark a century of written history of autism, the Autism Research Institute (ARI) has opened the National Autism History Museum—the first historical museum dedicated to autism. The four-room museum is located 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.

www.NationalAutismHistoryMuseum.com

Researchers report more evidence linking ASD, GI problems

(continued from page 1)

disorder," Bibiana Restrepo, Sandra L. Taylor, Matthew Dominic Ponzini, Kathleen Angkustsiri, Marjorie Solomon, Sally J. Rogers, Paul Ashwood, Daphne S. Say, Sonny Caceres, Shayan Alavynejad, Brianna Heath, David G. Amaral, and Christine Wu Nordahl, *Autism*, August 28, 2025. Address: Bibiana Restrepo, Division of Developmental and Behavioral Pediatrics, Department of Pediatrics, School of Medicine, University of California, Davis, 2825 50th Street, Sacramento, CA 95817, brestrepo@health.ucdavis.edu.

—and—

"Autistic children more likely to experience persistent stomach problems," news release, Nadine A. Yehya, University of California at Davis, September 17, 2025.

Need information on assessment?

Explore research, tools, and resources to support autism screening and assessment. Learn about:

- What assessment and evaluation mean
- The benefits of assessment and evaluation
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EDITORIAL: Stephen M. Edelson, Ph.D.

Invisible threats: the role of environmental toxins in autism

As our knowledge about autism continues to evolve, so does our understanding of its root causes. For many years, professionals blamed "refrigerator parents" and prescribed psychoanalytic therapy. Once the psychogenic theory was debunked, genetic research began to dominate autism science. Today, while we know that genes play a significant role in autism, we are beginning to recognize the critical importance of another factor: the environment (Rimland, 1964).

Currently, questions persist about the relative influence of genetics and environment on autism, with many people still viewing it as a purely genetic condition. However, as research findings mount, a clearer picture is forming. It is apparent that in many if not most cases, the condition arises from a complex interplay between genetic susceptibility and environmental influences (Hallmayer et al., 2011). Research increasingly shows that invisible yet potentially harmful substances can have long-lasting impacts on the fetus before birth and in the early stages of life, highlighting the need for us to take meaningful steps to reduce exposure to these substances—especially during crucial formative months in prenatal and early childhood development.

I believe it is time for the autism field to move beyond the vague use of the word "environment" and begin focusing on specific environmental toxins implicated in autism. Identifying and drawing attention to these toxins will help us to guide public policy, develop targeted interventions, and protect future generations of children.

I believe it is time for the autism field to move beyond the vague use of the word "environment" and begin focusing on specific environmental toxins implicated in autism. Identifying and drawing attention to these toxins will help us to guide public policy, develop targeted interventions, and protect future generations of children.

The interplay of genes and environment

When discussing the causes of autism, it is useful to frame the issue in terms of *genetic susceptibility* and *environmental influences*.

Genetic susceptibility helps to explain why many individuals exposed to the same environmental toxin may experience little or no effect, while a small portion develop long-term disabilities. It is likely that there is no specific "autism gene," but rather, a combination of genetic vulnerabilities that increase susceptibility to certain environmental influences. These vulnerabilities may affect systems such as the immune system, which protects the body from foreign substances, and the metabolic system, which affects the body's ability to detoxify harmful substances.

Environmental risk factors currently implicated by research

Controlled studies on the effects of human exposure to toxins are of course neither ethical nor feasible, and correlational studies can only suggest an association rather than a cause-and-effect relationship. For example, autism appears to be more common in cities than in rural areas; however, this does not necessarily indicate a causal link, as better access to diagnostic services in cities likely accounts for this pattern.

What adds credibility is that many of these risk factors show a *distance* or *dispersion* effect. The closer one is to a source—such as pesticides or particulate matter from vehicle exhaust—the higher the risk of autism (Shelton et al., 2014; Volk et al., 2011). In addition, replication by independent research groups in different regions of the country provides relatively strong evidence supporting a possible causal relationship (Becerra et al., 2013; von Ehrenstein et al., 2019).

Environmental toxins that currently are strongly implicated in autism (see Goines & Ashwood, 2013; Landrigan et al., 2012) include:

- **Air pollutants:** particulate matter, nitrogen dioxide, ozone, carbon monoxide.
- **Pesticides:** organophosphates, pyrethroids, permethrin, malathion, avermectin.
- **Metals:** lead, lithium, mercury, cadmium, aluminum, chromium, arsenic, manganese.
- **Plastics and industrial chemicals:** phthalates, bisphenol A, polychlorinated biphenyls (PCBs).

Patterns emerging from well-documented research

In addition to identifying environmental toxins that can alter fetal and early childhood development, it is important to understand the mechanisms by which they cause harm.

We know that when toxins enter the body, their effects depend on several factors, particularly the ability of the immune and metabolic systems to defend against them. In addition, the *level* of exposure is critical. This includes both the duration and amount of exposure, as well as the timing. For example, there is evidence suggesting that certain adverse neurological events may occur during the second trimester of pregnancy (Bilder, 2019).

Once toxic agents begin circulating in the body, they can trigger several well-documented biological processes linked to autism. These include brain inflammation (Vargus et al., 2005), oxidative stress (a marker of neuroinflammation; Usui et al., 2023), maternal immune activation (Ayoub, 2025; Usui et al., 2023), and disrupted cellular function. Naviaux (2020) has shown that cellular responses to toxins can initiate what is known as the *cell danger response*, in which the body enters a defensive state that can impair communication between cells.

Interestingly, emerging research indicates that the effects of particulate matter extend to the gut microbiome (Filardo et al., 2022). Exposure to particulate matter has been associated with disruptions in gut microbial balance that are also reported in autism, including reductions in microbial diversity (Fouladi et al., 2020; Kang et al., 2017). Furthermore, decreases in *Bacteroidetes* and *Lactobacillus*—both reported in autism—have also been associated with exposure to particulate matter (Li et al., 2023; Strati et al., 2017; Liu et al., 2021; Mihailovich et al., 2024).

Building on this understanding, a major study published earlier this year identified four distinct subtypes of autism (Litman et al., 2025; see ARRI 2025, Vol. 3). One subgroup, termed "broadly affected," was characterized by severe delays in reaching developmental milestones such as walking and talking, along with pronounced social-communication challenges and marked restrictive and repetitive behaviors. This subtype closely corresponds to what is often referred to as profound or severe autism (Lord et al., 2024). Notably, autism that arises in the context of maternal immune activation during pregnancy—which can be triggered by toxic exposures or infections—is also frequently described as severe or profound (Ellul et al., 2023).

What is very interesting is that both maternal immune activation profiles and *de novo* mutations were most prevalent in the "broadly affected" group. *De novo* mutations are not inherited from parents but instead arise spontaneously as errors during cellular replication, often occurring during

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Research Updates

Bone problems in ASD may be driven by lifestyle factors

Behavioral and lifestyle issues may negatively affect the bone health of children with autism spectrum disorders (ASD), according to a study by researchers in Australia and Canada.

Martin O'Flaherty and colleagues analyzed data on 66 children with ASD and 1,208 non-autistic controls, all between 11 and 12 years of age, who were participating in the Longitudinal Study of Australian Children. The researchers calculated the children's bone health, as well as the bone health of their parents, using peripheral quantitative computed tomography (pQCT) measurements of the tibial diaphysis (ankle) and metaphysis (shin).

The researchers report, "Our findings indicate poorer bone health as assessed by tibial pQCT among autistic children compared to non-autistic children at both the metaphysis and diaphysis. No differences in pQCT measures were found between parents of autistic and non-autistic children, suggesting no evidence of confounding by shared genetic or environmental factors."

These findings, the researchers say, are consistent with the findings of several other studies. For example, they note, a recent meta-analysis looking at differences in DXA [dual energy x-ray absorptiometry] measures of bone parameters between autistic and non-autistic children found substantially lower bone mineral density at the lumbar spine, hip, femoral neck, and total body in the autistic group.

The researchers say their findings indicate that "differences in bone health are likely driven by behavioral factors that are potentially amenable to intervention." One key factor, they say, is reduced physical activity, which mediated some of the difference in bone parameters they detected in a subsample analysis. Additional factors, they say, include restricted diets low in calcium and vitamin D, psychoactive medication use, and reduced exposure to vitamin D-producing sunlight. In addition, they say, "Nutritional deficiencies may be further exacerbated by the presence of gastrointestinal symptoms, which are more common among autistic children and may interfere with the absorption of key nutrients."

They conclude, "To make progress on improving bone health for autistic children and adolescents, further studies are needed to develop and test effective dietary and physical activity interventions for this population."

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"Bone health in autistic children: evidence from a population-representative Australian cohort study," Martin O'Flaherty, Sjaan Gomersall, Jessica Hill, Kathryn Fortnum, Matthew Bourke, John Cairney, Craig Munns, Peter Simm, and Marta Erlandson, *Journal of Autism and Developmental Disorders*, September 20, 2025 (free online). Address: Martin O'Flaherty, School of Human Movement and Nutrition Sciences and Health and Wellbeing Centre for Research Innovation, The University of Queensland, Brisbane, Australia, m.oflaherty@uq.edu.au.

Prenatal prescription opioid exposure not linked to ASD

Children of mothers who take prescribed opiate painkillers during pregnancy may not have an increased likelihood of developing autism spectrum disorders (ASD) or attention-deficit/hyperactivity disorder (ADHD), according to a study by researchers in Sweden, the United Kingdom, and the United States.

Emma Cleary and colleagues analyzed rates of ASD in more than 1.2 million children born in Sweden between 2007 and 2018, as well as rates of ADHD in more than 900,000 children born between 2007 and 2015. They also determined maternal levels of exposure to opioid pain medications during pregnancy.

They report, "At the population level, we replicated previous findings showing that risk of neurodevelopmental disorders increases as the dose, duration, and number of prescriptions increases." Two percent of the unexposed children had ASD by age 10, compared to 2.9% of children exposed to a low dose of opioids and 3.6% of children exposed to a high dose, with rates of ADHD following a similar pattern. However, they say, these associations "were substantially weakened or no longer present" when they controlled for a wide range of personal and familial factors, including genetic and environmental factors shared by siblings, and compared children whose mothers took prescribed opiates during pregnancy to children whose mothers took them before but not during pregnancy.

The researchers caution that their study population did not include mothers taking extremely high doses of opioids, or those taking the drugs for lengthy periods. However, Cleary says, "While this study is not able to rule out small increased risks with high amounts of exposure, the results suggest that there is not a causal effect of prescribed opioid analgesics on risk for two common neurodevelopmental disorders, providing more data to support decision-making."

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"Prescribed opioid analgesic use in pregnancy and risk of neurodevelopmental disorders in children: A retrospective study in Sweden," Emma N. Cleary, Ayesha C. Sujan, Martin E. Rickert, Franziska Fischer, Tyra Lagerberg, Zheng Chang, Paul Lichtenstein, Patrick D. Quinn, Anna Sara Öberg, and Brian M. D'Onofrio, *PLOS Medicine*, September 16, 2025 (free online). Address: Emma Cleary, Department of Psychological and Brain Sciences, Indiana University, Bloomington, Indiana 47405, encleary@iu.edu.

—and—

"Prescribed opioid pain medications during pregnancy likely aren't associated with increased risk of autism, ADHD," news release, *PLOS*, September 16, 2025.

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.

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.

—January 7, 2026—
EVIDENCE THAT SPEAKS: PRIORITIZING PROVEN COMMUNICATION SUPPORTS FOR NON-SPEAKING AUTISTIC CHILDREN
Connie Kasari, PhD

—January 14, 2026—
NUTRITION RESEARCH UPDATES: FIVE UNDERAPPRECIATED NUTRIENTS THAT NEURODIVERGENT KIDS MAY BE MISSING
Vicki Kobliner, MS, RDN

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Research Updates

Prenatal COVID exposure may increase odds of NDDs

A new study by researchers in the United States raises concerns about the effects of prenatal exposure to the SARS-CoV-2 virus that causes COVID-19.

Lydia Shook and colleagues analyzed data on more than 18,000 births occurring between March 1, 2020 and May 31, 2021 within the Mass General Brigham health system. The researchers compared the children of mothers who had any positive COVID-19 PCR laboratory test results during pregnancy to the children of mothers who had only negative test results. The hospital conducted universal COVID-19 screening during that time.

The researchers' analysis showed that maternal COVID-19 exposure in pregnancy was associated with a significant increase in neurodevelopmental diagnoses by the 36-month mark, "with effects most pronounced after third-trimester exposure and in male offspring." Sixteen percent of children exposed prenatally to COVID-19 received a neurodevelopmental diagnosis by the time they reached three years of age, compared to fewer than 10 percent of unexposed children. After accounting for multiple factors that could influence neurodevelopment, the researchers found that maternal COVID-19 infection during pregnancy was associated with a 29% higher likelihood of a child receiving a neurodevelopmental diagnosis by age three.

"These findings," senior study author Andrea Edlow says, "highlight that COVID-19, like many other infections in pregnancy, may pose risks not only to the mother, but to fetal brain development."

Shook comments, "Parental awareness of the potential for adverse child neurodevelopmental outcomes after COVID-19 in pregnancy is key. By understanding the risks, parents can appropriately advocate for their children to have proper evaluation and support."

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"Neurodevelopmental outcomes of 3-year-old children exposed to maternal SARS-CoV-2 infection in utero," Lydia L Shook, Victor Castro, Laura Ibanez-Pintor, Roy H. Perlis, and Andrea G. Edlow, *Obstetrics & Gynecology*, October 30, 2025 (online). Address: Andrea G. Edlow, Division of Maternal-Fetal Medicine, Dept. of Obstetrics & Gynecology, Massachusetts General Hospital, Boston, MA 02115, aedlow@mgh.harvard.edu.

—and—

"COVID-19 during pregnancy linked to higher risk of neurodevelopmental disorders in children," news release, Mass General Brigham, October 30, 2025.

Women with ASD report elevated rates of pain

Women with autism spectrum disorders (ASD) experience high rates of pain that can interfere with daily life, according to a survey by researchers in the United States.

Nathan Haid and colleagues surveyed 52 autistic adults assigned female at birth. Participants completed the Brief Pain Inventory, the Pain Anxiety Symptoms Scale (PASS-20), and the Generalized Anxiety Disorder Scale (GAD-7).

The researchers say, "We found that 65.4% of autistic AFAB [assigned female at birth] people in our sample reported pain in the last 24 hours. Although we did not directly compare autistic and non-autistic samples, in the National Health Interview Survey, only 22.1% of women reported pain most days of the week." In addition, the researchers say, the degree to which participants said pain interfered with their lives was comparable to that seen in chronic pain populations.

Study participants also reported high rates of both generalized anxiety and pain-related anxiety. Higher scores on the cognitive pain-related anxiety subscale of the PASS-20—which measures anxiety related to rumination and fixation on pain—were associated with an increase in generalized anxiety as well as an increased impact of pain on daily life.

The researchers conclude that autistic women "are experiencing high rates of pain, pain interference, anxiety, and pain-related anxiety," adding, "Given the relationship between pain and anxiety reported for autistic women, therapies that specifically target pain-related anxiety may have profound impacts on autistic women's quality of life."

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"Autistic women report high levels of pain, pain-related anxiety, and pain interference," Nathan W. Haid, Michelle D. Failla, and Alexandra Sturm, *Pain Reports*, December 2025 (free online). Address: Alexandra Sturm, Loyola Marymount University, 1 LMU Dr., Suite 4700, Los Angeles, CA 90045, Alexandra.sturm@lmu.edu.

Are you an adult with autism?

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

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

Men with Parkinson's have higher rate of ASD features

Men with Parkinson's disease (PD) or other motor disorders exhibit an elevated rate of autistic features, according to a study by researchers in India and the United Kingdom.

Ipsita Dey and colleagues note that PD and related disorders are reported to be three times more common in adults with autism spectrum disorders (ASD) than in the general population. However, they say, "While initial reports have demonstrated greater PD traits in older autistic individuals, the converse has not been directly tested, that is, autistic symptoms have not been investigated in PD patients."

To address this issue, the researchers administered a test of autistic traits to 330 participants. One-third of the group was diagnosed with PD, one third had other motor disorders, and one-third had no motor or neurological conditions.

The researchers say, "Higher autistic traits were noted in both Parkinson's disease and other motor disorder groups compared to the typically aging controls, suggesting an association between motor disorders and dimensional autistic traits. Exploratory analyses revealed a clear pattern of results in males, where Parkinson's disease was associated with the highest autistic traits, followed by the other motor disorders, and then by the typically aging group." However, women with PD or other motor diseases did not differ in autistic traits from controls.

The researchers conclude, "This new evidence suggests a sex-specific overlap between these conditions and highlights the need for accounting for elevated autistic features in planning support for males with Parkinson's disease and other movement disorders."

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"Elevated autistic features in Parkinson's disease and other motor disorders," Ipsita Dey, Swarnima Pathak, Sreerupa Chakrabarty, Matthew K Belmonte, Supriyo Choudhury, Hrishikesh Kumar, and Bhismadev Chakrabarti, *Autism*, August 26, 2025 (free online). Address: Bhismadev Chakrabarti, Centre for Autism, School of Psychology and Clinical Language Sciences, University of Reading, Reading RG6 6ES, UK, b.chakrabarti@reading.ac.uk.

ARI continues to receive Charity Navigator's four-star (highest) rating, a "Platinum" rating for transparancy from Guidestar, and a "Top Rated" badge from Great NonProfits.

Standard exercise guidelines may fall short in meeting the needs of many individuals with ASD

While increasing evidence indicates that exercise significantly benefits individuals with autism spectrum disorders (ASD), researchers in the United States say that federally endorsed exercise guidelines—exemplified by the FITT (Frequency, Intensity, Time, Type) principle—"fail to account for neurodevelopmental, motor, and sensory differences across the autism spectrum."

David Geslak and colleagues say that the frequency of exercise recommended by FITT is unrealistic for many autistic individuals. For instance, they note that children with ASD typically are already involved in other therapies for many hours each week, limiting time for exercise, and that their schools may not have physical education programs equipped to accommodate them. Instead, they recommend creating a flexible schedule that includes one to three days per week of exercise, depending on an individual's ability and need for support.

Also, rather than relying on standard measurements of intensity, they say that providers should acknowledge that "meaningful outcomes do not require high levels of exertion, and in many cases, lower-intensity movement may be both more accessible and more beneficial." They stress the importance of individualizing exercise intensity guidelines, noting that stereotypic behaviors, motor coordination challenges, and other issues can make moderate to vigorous activity difficult for individuals with ASD. They also suggest that practitioners working with individuals who have language impairments use pictorial measures rather than standard guidelines when assessing the perceived intensity of exercise.

The researchers add that while standard guidelines recommend fairly long intervals of exercise, "emerging evidence suggests 10 to 15 minutes of exercise provides initial health benefits in autistic individuals and should be considered a realistic introduction to exercise. A starting goal of 10 to 15 minutes is realistic and achievable, not only for the individual but also for caregivers, exercise professionals, and/or PE/APE [adaptive physical education] teachers."

Noting that standard guidelines focus primarily on aerobic activity, the researchers say this can be problematic for individuals with autism, who often have motor impairments and additional challenges that make aerobic exercise difficult. Instead, they say, "exercises that focus on muscular strength, muscular endurance, and flexibility may offer a more accessible starting point and improve outcomes."

When developing an exercise program for an individual with ASD, the researchers say, the first step should be to take the interests, abilities, and overall health of the individual into account. Once a program begins, they say, practitioners should continuously evaluate the individual's response to the type, frequency, intensity, and length of the activities; modify the program to account for sensory sensitivities and other individual needs; and obtain regular feedback from participants or caregivers to determine if the program is meeting their needs or requires revision.

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"Exercise as medicine across the autism spectrum: a conceptualized framework," David S. Geslak, Robyn T. Boudreaux, and Benjamin D. Boudreaux, *Current Sports Medicine Reports*, August 2025 (online). Address: David S. Geslak, Exercise Connection, Lisle, IL 60532, david@exerciseconnection.com.

Editorial: Invisible threats: the role of environmental toxins in autism (continued from page 3)

early embryonic development. Their occurrence can be influenced by factors such as advanced parental age—a well-documented risk for both mothers and fathers (Croen et al., 2007)—as well as environmental exposures that disrupt genomic stability (Pugsley et al., 2022).

This raises an important question: Could many individuals who are severely affected by autism represent cases in which toxic exposures during pregnancy trigger maternal immune activation and simultaneously contribute to the emergence of *de novo* mutations? Research exploring this possibility is urgently needed, as it may be relevant to more than one-quarter of the autism population (Hughes et al., 2023).

Cleaning up pollution in the air, water, and soil is an enormous undertaking and often prohibitively expensive, but there are many practical and cost-effective steps we can take.

In a related ongoing research project, Judith Miller, a clinical psychologist at the Children's Hospital of Philadelphia, is conducting a comprehensive study of environmental factors to which individuals are exposed over time. She is leading a multiyear project that integrates genomic and exposomic data (the latter focusing on lifetime exposures to environmental factors) from more than 100,000 children, including about 4,000 autistic children, and links this data to detailed maternal health records. The study incorporates geospatial data on air and water quality, green space access, and a wide range of other environmental exposures to explore how genetic susceptibility and environmental context may interact in autism.

Final thoughts

Can we realistically reduce harmful exposures when they are so deeply tied to economic and political forces? Cleaning up pollution in the air, water, and soil is an enormous undertaking and often prohibitively expensive, but there are many practical and cost-effective steps we can take.

In the near term, the highest priority should be protecting those most vulnerable: pregnant women and very young children. One promising effort in this area is P2i (Preconception to Infancy), a new initiative launched by the Northwest Autism Foundation. This comprehensive program is designed to support couples from the preconception stage through their children's infancy, with the goal of promoting safer pregnancies and fostering healthier early development. One of the key goals of P2i is to reduce the body burden of toxic chemicals in mothers and their children.

There also is growing interest in interventions to reduce the harmful effects of environmental toxic exposures in autism. Strategies focus on enhancing detoxification pathways, such as increasing glutathione synthesis and strengthening antioxidant defenses. Additional approaches that support mitochondrial function, lower oxidative stress, and modulate immune responses may further reduce toxicant burden and its neurodevelopmental impact (see Rossignol & Frye, 2012).

Given the importance of efforts such as these, I believe it is time for the autism field to speak more openly and directly about specific environmental toxins and exposures. Greater transparency about these risk factors—such as exposure to certain heavy metals, pesticides, air pollutants, and prenatal stressors—will foster better public understanding and help guide prevention and policy efforts.

Researchers and clinicians have a responsibility to communicate emerging evidence clearly and without unnecessary delay. Open dialogue among scientists, policymakers, and the public will accelerate progress toward reducing harmful exposures and improving outcomes for future generations.

References available at www.ARRIReferences.org.

ARRI Statement on Prenatal Acetaminophen Use, Leucovorin, and Autism

The Autism Research Institute (ARI) provides the following statement in response to recent media inquiries regarding potential connections between prenatal acetaminophen use, leucovorin supplementation, and autism spectrum disorders (ASD).

ARI's Commitment to Evidence-Based Research

ARI is committed to monitoring ongoing research and sharing accurate, evidence-based information with autistic people, families, researchers, and policymakers. This includes addressing questions about environmental influences and potential medical factors, such as the use of over-the-counter medications.

"We know there are subtypes of autism, with no single cause explaining the condition and no single intervention benefiting everyone on the spectrum. Research should focus on understanding these differences rather than generalizing findings to every autistic individual," said ARI Chief Science Officer, Dr. Steve Edelson. "By identifying unique biological, developmental, and environmental factors within each subtype, we can begin to develop more targeted, effective approaches."

Acetaminophen Research

The Autism Research Institute acknowledges that recent studies have examined potential associations between prenatal acetaminophen (commonly known as Tylenol in the U.S.) exposure and autism. While these studies contribute to our understanding of possible risk factors, ARI maintains that the current evidence does not establish a definitive causal relationship between acetaminophen use during pregnancy and autism.

Extensive studies, including a 2024 Swedish study analyzing nearly 2.5 million births, suggest that observed associations between prenatal acetaminophen use and autism may reflect familial confounding rather than a direct causal link. Research led by Dr. Mady Hornig of Columbia University underscores the complexity of these factors. Her work highlights the role of maternal immune responses and fever, showing that inflammation during pregnancy may affect neurodevelopment independently of medication use. Preliminary evidence also indicates that acetaminophen taken to reduce fever may be neutral—or even potentially protective—though these findings remain inconclusive.

Leucovorin (Folinic Acid) Research

ARI has supported Dr. Richard Frye's research related to leucovorin (folinic acid) as a potential intervention in autism, particularly for individuals with metabolic differences such as impaired methylation or glutathione production. We are encouraged by the preliminary results suggesting that leucovorin supplementation may benefit certain subgroups of individuals with autism spectrum disorders.

Dr. Frye's work represents potential progress in understanding possible biomarker-based approaches to intervention. However, we emphasize that this research is still evolving, and larger, controlled studies are needed to fully validate these findings and establish optimal treatment protocols.

It is important to note that Dr. Frye's leucovorin research explores potential therapeutic interventions rather than causative factors and should not be interpreted as supporting any specific theory about acetaminophen causation.

Ongoing Commitment

ARI remains committed to supporting rigorous, scientifically sound research into all aspects of autism spectrum disorders. We encourage:

- Continued investigation of the interplay between genetic susceptibility, environmental factors, and critical developmental periods.
- Well-controlled studies that distinguish association from causation.
- Investigation of maternal immune responses and inflammation as pathways to neurodevelopmental differences.
- Research that includes autistic people and focuses on appropriate medical care.
- Transparent communication about both the promise and limitations of emerging research.

Individuals, parents and healthcare providers are encouraged to make medical decisions based on established guidelines and consultation with qualified professionals, while staying informed about ongoing research developments. As Dr. Hornig notes, untreated fever during pregnancy carries known risks, and decisions regarding fever-reducing medications should be made carefully with medical guidance.

"Autism is complex, and much remains to be learned," Dr. Edelson said. "As always, ARI is committed to following the evidence wherever it leads and to providing clear, trustworthy information as new knowledge emerges."

Child neurologists often fail to identify motor problems in children with autism

Many children with autism spectrum disorders (ASD) exhibit significant impairments in motor skills, but a new study by U.S. researchers indicates that neurologists—who often play a major role in the medical care of people with ASD—frequently fail to identify these impairments.

Harika Kottakota and colleagues conducted an anonymous survey of 100 child neurologists, asking them about their awareness of motor impairments in pediatric patients with ASD and their clinical approach to addressing these impairments. They report, "We found most child neurologists were not confident that motor impairments were an associated feature of ASD, do not frequently evaluate for motor impairments, lack sufficient tools for motor evaluations with autistic children, face multiple barriers to providing interventions, and do not receive adequate clinical training regarding this topic."

Overall, only 36% of respondents recognized motor deficits as an associated feature of autism, and more than half underestimated how common these impairments are. Many remarked that behavioral barriers or time constraints made it difficult to assess children with ASD for motor problems. Study coauthor Rujuta Wilson says, "Motor concerns are just as common, if not more common, than verbal language difficulties in children with autism, yet they're being significantly under-recognized and undertreated."

The researchers note that motor problems often emerge in infancy and can have a cascading effect on children's cognitive, physical, and social development. In addition, they point out that there are strategies for addressing these problems once clinicians identify them. To increase the chances that problems are detected early, Wilson says, "We need to ensure that training on the assessment of unique motor difficulties in autistic individuals is well developed during medical school and residency training."

—

"Survey of child neurologists highlights a missed opportunity for identifying and treating motor impairments in autism," Harika Kottakota, Emily Hotez, and Rujuta B. Wilson, *Pediatric Neurology*, October 2025 (online). Address: Rujuta Wilson, UCLA Center for Autism Research and Treatment, Semel Institute for Neuroscience and Human Behavior, Los Angeles, California 90095, rbhatt@mednet.ucla.edu.

—and—

"Survey shows only 36% of neurologists identify motor deficits as part of autism diagnosis," news release, University of California at Los Angeles, October 14, 2025.

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—About ARI—

The Autism Research Institute (ARI) is the oldest autism research organization in the world, founded by Dr. Bernard Rimland in 1967.

ARI'S WORK INCLUDES:

Conducting and sponsoring research on the causes of and best treatments for autism ($733,000 in research grants awarded last year), with a focus on research that can translate rapidly into help for today's autistic children and adults and their families.

•

Networking researchers, physicians, and parents to speed the development and dissemination of safe and effective treatment methods.

•

Hosting webinars and one of the largest informational websites on autism in the world.

•

Sponsoring think tanks where researchers and experienced clinicians can share their knowledge.

ARI's work relies on charitable contributions from individuals and organizations. All donations are tax deductible. We are proud to have earned Charity Navigator's highly respected "Four Star Award" for fiscal management, accountability, and transparency.

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