

Autism Research Review

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

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

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

New multi-national study adds to evidence linking alterations of the gut microbiome to ASD

Strong new evidence linking alterations of the gut microbiome to autism spectrum disorders (ASD) comes from a new multi-national study by James Morton and colleagues.

In the study, researchers in North America, South America, Europe, and Asia developed an algorithm to re-analyze 25 datasets containing information on autistic and neurotypical controls. The datasets included 10 microbiome datasets and 15 other datasets

Rob Knight, a coauthor of the study, says, “Before this, we had smoke indicating the microbiome was involved in autism, and now we have fire.”

containing information on dietary patterns, products of cell metabolism, cytokine profiles, and human brain gene expression profiles. Within each dataset, the algorithm found the best matched pairs of autistic and neurotypical individuals based on age and sex.

“Rather than comparing average cohort results within studies,” study coauthor Gaspar Taroncher-Oldenburg says, “we treated each pair as a single data point, and thus were able to simultaneously analyze over 600 ASD-control pairs corresponding to a de facto cohort of over 1,200 children.” This allowed them to reliably identify microbes that differed in abundance between individuals with ASD and neurotypical controls.

The researchers say their analysis identified autism-specific metabolic pathways associated with specific human gut microbes. These pathways correlated with brain gene expression changes, restrictive dietary patterns, and pro-inflammatory cytokine profiles seen in individuals with ASD. “We hadn’t seen this kind of clear overlap between gut microbial and human metabolic pathways in autism before,” Morton says.

He adds, “We were able to harmonize seemingly disparate data from different studies and find a common language with which to unite them. With this, we were able to identify a microbial signature that distinguishes autistic from neurotypical individuals across many studies.”

Importantly, the researchers detected an overlap between microbes associated with autism and those identified in a long-term fecal microbiota transplant study led by James Adams and Rosa Krajmalnik-Brown (see ARRI 2023, No. 1). Commenting on the findings, Krajmalnik-Brown (who was not involved in the current study) says, “Another set of eyes looked at this, from a different lens, and they validated our findings.”

Rob Knight, a coauthor of the current study, says, “Before this, we had smoke indicating the microbiome was involved in autism, and now we have fire.”

“Multi-level analysis of the gut-brain axis shows autism spectrum disorder-associated molecular and microbial profiles,” James T. Morton, Dong-Min Jin, Robert H. Mills, Yan Shao, Gibraan Rahman, Daniel McDonald, Qiyun Zhu,

Metin Balaban, Yueyu Jiang, Kalen Cantrell, Antonio Gonzalez, Julie Carmel, Linoy Mia Frankienstajn, Sandra Martin-Brevet, Kirsten Berding, Brittany D. Needham, Maria Fernanda Zurita, Maude David, Olga V. Averina, Alexey S. Kovtun, Antonio Noto, Michele Mussap, Mingbang Wang, Daniel N. Frank, Ellen Li, Wenhao Zhou, Vassilios Fanos, Valery N. Danilenko, Dennis P. Wall, Paúl Cárdenas, Manuel E. Baldeón, Sébastien Jacquemont, Omry Koren, Evan Elliott, Ramnik J. Xavier, Sarkis K. Mazmanian, Rob Knight, Jack A. Gilbert, Sharon M. Donovan, Trevor D. Lawley, Bob Carpenter, Richard Bonneau, and Gaspar Taroncher-Oldenburg, *Nature Neuroscience*, June 26, 2023 (free online). Address: Gaspar Taroncher-Oldenburg, gtaroncher@gmail.com.

—and—
 “New research clarifies connection between autism and the microbiome,” news release, Susan Reslewic Keatley, Simons Foundation, June 26, 2023.

Prenatal exposure to cannabis may increase likelihood of ASD

Cannabis use during pregnancy may alter placental and fetal DNA methylation (the process of turning genes “on” and “off”) in ways that increase the likelihood of autism spectrum disorder (ASD) or other neurobehavioral conditions, according to a new study.

Lyndsey Shorey-Kendrick and colleagues, who conducted the study, say,

The researchers found that THC exposure altered fetal and placental methylation, causing significant changes involving genes associated with neurobehavioral disorders including ASD.

“Cannabis use among pregnant individuals, especially during the critical developmental window in the first trimester to mitigate morning sickness symptoms, has doubled in the past decade, and half of those that use cannabis will continue to use throughout pregnancy.” They add that while research is limited, “[S]tudies suggest adverse effects of prenatal cannabis exposure that include preterm birth, stillbirth, and small for gestational age infants. Maternal cannabis use has also been associated with an increased risk for neurobehavioral morbidity in hu-

man offspring, including ASD, attention deficit hyperactivity disorder (ADHD), intellectual disability and learning disorders, and other neuropsychiatric disorders.”

To explore the effects of cannabis exposure *in utero*, Shorey-Kendrick and colleagues studied pregnant rhesus macaques. Half of the animals received a daily edible of THC (the active ingredient in cannabis), while the other half received a placebo. The researchers found that THC exposure altered fetal and placental methylation, causing significant changes involving genes associated with neurobehavioral disorders including ASD.

Study coauthor Jamie Lo, who notes that “it’s not common practice for providers to discuss cannabis use with patients who are pregnant or trying to conceive,” says the researchers hope their findings will open up a broader dialog about the potential effects of cannabis use during preconception and the prenatal period.

“Prenatal delta-9-tetrahydrocannabinol exposure is associated with changes in rhesus macaque DNA methylation enriched for autism genes,” Lyndsey E. Shorey-Kendrick, Victoria H. J. Roberts, Rahul J. D’Mello, Elinor L. Sul-

continued on page 2

Sensory issues may be a factor in substance use in individuals with ASD

Sensory issues may play a role in elevated levels of substance abuse in individuals with autism spectrum disorders (ASD), according to a new study from the Netherlands.

Frank van den Boogert and colleagues note, “ASD is considered to be a risk factor for substance abuse, with six times higher risk of substance abuse in persons with ASD in comparison with persons without autistic traits.” However, they say, “Although the association between autism spectrum disorder and substance use has been extensively researched, this is not the case for the possible association between sensory processing difficulties and substance use.”

The researchers asked 101 adults with ASD to fill out two questionnaires, the Adolescent/Adult Sensory Profile and the Alcohol Use Disorders Identification Test – Consumption. They divided participants into

The researchers found that “sensory processing difficulties are associated with alcohol use in adults with ASD,” but say further research is needed to determine if these individuals are “self-medicating” or have other neurobiological vulnerabilities to substance use.

four sensory categories: sensory seeking, sensory sensitivity, sensory avoiding, and low registration (reflecting a high sensory threshold and low levels of responding). They also broke participants into three categories: non-drinkers, non-hazardous drinkers, and hazardous drinkers.

The researchers report that “sensory processing difficulties are associated with alcohol use in adults with ASD.” Drinkers reported higher levels of low registration, non-hazardous drinkers reported higher levels of sensory sensitivity, and hazardous drinkers reported higher levels of sensory seeking in comparison with non-drinkers.

The researchers say, “Substance abuse in ASD might in part be explained by sensory processing difficulties.” They add, “Whether alcohol is used as ‘self-medication’ or is associated with other neurobiological vulnerabilities needs further investigation in larger follow-up studies.”

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 “Sensory processing and alcohol use in adults with autism spectrum disorder,” Frank van den Boogert, Bram Sizoo, Yvonne H.A. Bouman, Witte J.G. Hoogendijk, and Sabine J. Roza, *Alcohol*, August 19, 2023 (free online). Address: Sabine J. Roza, Department of Psychiatry, Erasmus MC, Dr. Molewaterplein 40, 3015 GD, Rotterdam, the Netherlands, s.roza@erasmusmc.nl.

Animal study reveals clues that developmental vitamin D deficiency may be associated with gut alterations in autism

Vitamin D deficiency is strongly implicated as a risk factor for autism spectrum disorders (ASD), and researchers in Australia report evidence that vitamin D deficiency during early development may increase the likelihood of ASD by altering the gut.

Man Kumar Tamang and colleagues note that growing numbers of both animal and human studies indicate an association between autism and gastrointestinal issues. In addition, they say, vitamin D deficiency and/or supplementation is known to affect the structure, function, and microbiome of the gut. “Thus,” they say, “our objective in this study was to examine if the gut microbiome and gut physiology were... altered by developmental vitamin D deficiency and whether any alterations were associated with ASD-related behavioral phenotypes.”

As in previous studies by the same team, the researchers observed a range of ASD-related behaviors in rats with developmental vitamin D deficiency. These included altered dam-pup communication, reduced social interaction, and increased stereotypical behaviors. In addition, they detected “significant impacts of developmental vitamin D deficiency on gut health.” These included alterations of the gut microbiome and decreased length of villi (the finger-like projections on the interior surface of the small intestine).

The researchers also found increased levels of a short-chain fatty acid (SCFA)

called propionate in the ileum. Previous research has suggested an association between elevated levels of propionate and autism in humans.

They conclude, “The epidemiological links between maternal vitamin D deficiency and increased autism risk are well-established. The emerging data concerning gut health in children with autism and the role of vitamin D in preserving gut function suggest this ASD risk factor may act via alterations to the gut microbiota, gut SCFA synthesis, or altering gut physiology. The high prevalence of vitamin D deficiency in pregnant women increases concern regarding this link.”

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 “Developmental vitamin D-deficiency produces autism-relevant behaviours and gut-health associated alterations in a rat model,” Man Kumar Tamang, Asad Ali, Renata Nedel Pertile, Xiaoying Cui, Suzy Alexander, Marloes Dekker Nitert, Chiara Palmieri, and Darryl Eyles, *Translational Psychiatry*, June 14, 2023 (free online). Address: Darryl Eyles, Queensland Brain Institute, The University of Queensland, Brisbane, Australia, d.eyles@uq.edu.au.

Prenatal cannabis exposure may increase odds of ASD

(continued from page 1)

livan, Susan K. Murphy, Owen J. T. Mccarty, Danny J. Schust, Jason C. Hedges, A. J. Mitchell, Jose Juanito D. Terrobias, Charles A. Easley IV, Eliot R. Spindel, and Jamie O. Lo, *Clinical Epigenetics*, July 6, 2023 (free online). Address: Lyndsey Shorey-Kendrick, Division of Neuroscience, Oregon National Primate Research Center, Oregon Health and Science University, Beaverton, OR, 97006, shorey@ohsu.edu.

—and—
 “THC use during pregnancy linked to changes in fetal development,” news release, Nicole Rideout, Oregon Health & Science University, July 6, 2023.

—IN MEMORIAM— Donald Triplett

Donald Triplett, who was the first person to be officially diagnosed with autism, has passed away at the age of 89.

Triplett, who became famous as “Case 1” in Leo Kanner’s groundbreaking 1943 paper on autism, was diagnosed by Kanner when he was five years old. As a toddler, Triplett could sing many tunes accurately and had an extraordinary memory for names and faces. He also exhibited perfect pitch. Kanner said of him, “When in a room, he completely disregarded the people and instantly went for objects, preferably those that could be spun.”

Triplett worked for nearly 65 years at the Mississippi-based Bank of Forest, which was cofounded by his maternal grandfather. His life was the subject of *In a Different Key: The Story of Autism*, by John Donvan and Caren Zucker, as well as a PBS documentary by the same name.

Dealing with self-injurious behaviors?

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

autism.org/self-injury

EDITORIAL: Stephen M. Edelson, Ph.D.

Revisiting Two Lesser-Known Teaching Strategies to Enhance Speech Production in Autism

In this editorial, I would like to shed light on two methods for improving the speech production of individuals on the autism spectrum, discuss potential neurological factors that may underlie their effectiveness, and encourage the autism community to re-evaluate them. The first method, commonly known as “simultaneous communication,” combines the teaching of sign language with verbal speech. The second strategy focuses on prompting spontaneous speech through vestibular stimulation using a therapeutic platform swing. Occasionally discussed by therapists but now less popular, these approaches could present fresh opportunities to enhance speech and overall communication abilities in many autistic individuals, warranting further research.

Background: Speech Issues in ASD

A significant proportion of individuals with autism either are non-verbal or have limited verbal skills, with estimates ranging between 25 and 30 percent (1). In the past, these individuals were frequently labeled with “elective mutism,” implying a deliberate decision not to speak, especially when observed speaking intermittently in high-stress situations (2,3). This perspective is rooted in early theories on autism suggesting that parental neglect or emotional trauma causes the condition, leading children to refrain from communicating with their parents (2).

Today, there is general consensus that the speech production difficulties of autistic individuals are not a matter of choice but are based on physiological factors. Neurological research, including studies on neural activity and post-mortem tissue, indicates that several brain regions could be responsible for these issues, such as Broca’s and Wernicke’s areas (4,5), among other regions. The variability in impairment across these regions in different individuals could account for the diverse language challenges observed in autism. In addition, sensory overload in one or more senses can inhibit speech, as an individual becomes overwhelmed with discomfort or pain, either externally or internally, instead of communicating with others.

Neural plasticity is the brain’s ability to change and adapt based on experience (6). This includes the ability to learn new skills, such as speech (7). This inherent flexibility of the brain could pave the way for effective therapeutic interventions. Such interventions may leverage movement experiences,

suggesting that these activities might stimulate or even activate certain neural pathways.

Simultaneous Communication and Speech

Simultaneous communication, also known as “signed speech” and “total communication,” has received a respectable amount of attention from behavioral researchers (8-10). This teaching method involves using hand movement or gestures, including American Sign Language and Signing Exact English, in conjunction with traditional speech therapy—for instance, signing the word “drink” while simultaneously saying the word out loud.

Simultaneous communication was once popular among behavioral researchers and therapists. Initial studies highlighted its advantages, especially for those capable of imitating verbal sounds, compared to speech therapy alone. During my three years working with Dr. Ivar Lovaaas at UCLA’s Young Autism Project in the late 1970s, I discussed with him the value of combining sign language and speech. He stated that the research clearly showed that it was helpful in many cases, but a number of therapists and parents were reluctant to adopt this method, concerned it might inhibit the development of verbal speech.

A popular approach today is the Picture Exchange Communication System (PECS), an alternative augmentative communication method rooted in Applied Behavior Analysis. PECS involves teaching individuals to use pictures for conveying needs or intricate ideas, and in some cases, it has led to the development of speech (11).

There is some debate about whether teaching speech through sign language is more effective than using PECS. One study showed that training in sign language led to greater vocalizations compared to PECS training (12). Some advocates of PECS question the value of teaching sign language, pointing out that motor skill difficulties may hinder many autistic individuals from producing signs (13). Yet, considerable research suggests that many autistic individuals can use a form of sign language, even if it is rudimentary in nature (14).

From a neurological standpoint, sign language and speech production utilize overlapping brain structures. Both stimulate linguistic processing regions in the left hemisphere, including Broca’s and Wernicke’s areas, which are recognized to be affected in autism (4,5). However, engaging

in sign language also involves visual and spatial processing areas (15-17).

Introducing music during simultaneous communication training sessions might enhance both sign language and speech production. In a study with 10 autistic children, every child showed better imitation when exposed to a musical setting compared to a rhythm-only scenario (18). Wan et al. propose that musical interventions could link brain regions associated with language processing to auditory areas, such as the arcuate fasciculus and the uncinate fasciculus (19).

Vestibular Stimulation and Speech

After many clinical observations of heightened vocalizations among clients while undergoing sensory therapy on a platform swing at a renowned treatment center in Glendale, Arizona, therapists decided to record the verbal expressions of a minimally verbal nine-year-old autistic child (20). Five-minute recordings were made five minutes before, during, and five minutes after the child received vestibular stimulation on the platform swing each day for a span of four weeks. Analysis showed that the child, on average, vocalized 17.0 words during the swing sessions, in contrast to 2.0 words before and 1.3 words after the sessions.

In a similar study, investigators examined vestibular stimulation’s effects on preschoolers with developmental delays. They also reported enhanced spontaneous language immediately after stimulation sessions (21).

Vestibular stimulation has been linked to visuospatial skills, including spatial memory, mental rotation, and the mental visualization of three-dimensional space. All of these are important factors when learning sign language (22).

Moreover, heightened vocalization could stem from the stimulation of the posterior cerebellum, a region tied to vestibular activity (23). Studies have shown that this particular brain area is compromised in autism (24) and plays a role in language processing (25).

Conclusion

While simultaneous communication and vestibular stimulation require additional scientific investigation, both methods show promise. These approaches, once popular in autism therapy but now not as widely adopted, could unlock new avenues for enhancing speech production and overall communication abilities in many autistic individuals.

References are available at
www.ARRIReferences.org.

Research Updates

Animal study adds to evidence of link between pyrethroids, autism

A new animal study adds to evidence that prenatal exposure to common insecticides called pyrethroids may increase the likelihood of a child developing autism or another neurodevelopmental disorder.

Melissa Curtis and colleagues, who authored the study, note that earlier research has implicated pyrethroid exposure as a risk factor for autism, developmental delay, and neurodevelopmental disorders in general. They note, "Analysis of data from the CHARGE [Childhood Autism Risks from Genetics and the Environment] study showed a significant increase in risk for either ASD [autism spectrum disorder] or developmental delay from exposure during pregnancy to pyrethroid pesticides being applied up to 1.5 kilometers from the home. A regional study in New York showed an association between areas where aerial application of pyrethroid pesticides was used, and ASD and developmental delay prevalence in the area. Additionally, the presence of pyrethroid metabolites in blood or urine correlates with risk for ADHD in children."

In their own study, Curtis and colleagues investigated the effects of the pyrethroid chemical deltamethrin on the offspring of female mice exposed to the chemical during pregnancy or lactation. The researchers found that in addition to exhibiting alterations in the dopamine system in their brains, exposed mice had elevated levels of hyperactivity and repetitive behaviors, reduced vocalizations, and an increased likelihood of learning difficulties.

Study coauthor James Burkett says the symptoms of the offspring of exposed mice are similar to those exhibited by humans with neurodevelopmental disorders. He adds, "We're not implying that these mice have autism or ADHD.... What we're suggesting is that exposure to this insecticide has altered something in their brain, resulting in the same patterns of behavior that we witness in children with autism."

Burkett comments, "Someone who comes and sprays in your house is most likely using [a pyrethroid insecticide]. It's employed in landscaping, and for mosquito fogging in streets. It's ubiquitous. Nonethe-

less, our research further substantiates the notion that these substances may not be as harmless for kids and expectant mothers as we formerly assumed."

"Developmental pyrethroid exposure causes a neurodevelopmental disorder phenotype in mice," Melissa A. Curtis, Rohan K. Dhamsania, Rachel C. Branco, Ji-Dong Guo, Justin Creeden, Kari L. Neifer, Carlie A. Black, Emily J. Winokur, Elissar Andari, Brian G. Dias, Robert C. Liu, Shannon L. Gourley, Gary W. Miller, and James P. Burkett, *PNAS Nexus*, April 25, 2023 (free online). Address: James Burkett, james.burkett@utoledo.edu.

—and—

"Research links common insecticide to neurodevelopmental disorders," news release, University of Toledo, April 25, 2023.

Study detects significant memory problems in ASD

Many children with autism spectrum disorders (ASD) have difficulty remembering faces, and a new study suggests that they have additional memory problems that may impact their behavior and learning.

Jin Liu and colleagues compared 25 children with high-functioning autism and normal IQs to a control group of 29 typically developing children. All of the children were between 8 and 12 years of age.

The researchers tested the children's memory skills, including their ability to remember faces, written material, and photographs lacking social content. They analyzed the children's ability to recognize information they had previously seen or heard, as well as their ability to recall information by describing or reproducing details they had seen or heard. Participants also underwent functional magnetic resonance imaging (fMRI) to measure functional connectivity in brain regions involved in memory.

As expected, children with ASD were poorer than typically developing children at remembering faces. Unexpectedly, however, their scores for immediate and delayed verbal recall, immediate visual recall, and delayed verbal recognition of non-social material were lower than those of controls.

Liu says, "The study participants with autism had fairly high IQ, comparable to typically developing participants, but we still observed very obvious general memory impairments in this group." In addition, the researchers found that facial memory and non-social memory skills were less consistent in the group with ASD. Liu comments, "Among children with autism, some kids seem to have both impairments and some have more severe impairment in one area of memory or the other."

The researchers say the memory problems they detected may put children with ASD at a disadvantage academically as well as impacting their social skills. Study coauthor Vinod Menon comments, "Social cognition cannot occur without reliable memory. Social behaviors are complex, and they involve multiple brain processes, including associating faces and voices to particular contexts, which require robust episodic memory. Impairments in forming these associative memory traces could form one of the foundational elements in autism."

fMRI scans showed that for children with ASD, the ability to retain non-social memories was predicted by connections in a network involving the hippocampus, a structure that helps to regulate memory. However, the memory for faces in these children was predicted by a separate set of connections centered on the posterior cingulate cortex, which plays roles in social cognition and the ability to distinguish oneself from other people. In both networks, the brains of children with autism showed over-connected circuits relative to the brains of typically developing children.

Menon says, "The findings suggest that general and face-memory challenges have two underlying sources in the brain which contribute to a broader profile of memory impairments in autism."

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"Replicable patterns of memory impairments in children with autism and their links to hyperconnected brain circuits," Jin Liu, Lang Chen, Hyesang Chang, Jeremy Rudoler, Ahmad Belal Al-Zughoul, Julia Boram Kang, Daniel A. Abrams, and Vinod Menon, *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, May 15, 2023 (online). Address: Vinod Menon, Department of Psychiatry & Behavioral Sciences, Stanford University School of Medicine, Stanford, California 94305, menon@stanford.edu.

—and—

"Children with autism have broad memory difficulties, new study finds," news release, Erin Digitale, Stanford University Medical Center, July 10, 2023.

Need help or information?

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

New to autism?

If so, the Autism Research Institute has valuable information on seeking appropriate medical care. For a list of important questions to ask a potential medical provider, see:

<https://www.autism.org/>

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Research Updates

Placental inflammation may increase likelihood of ASD

Placental inflammation during pregnancy may increase the likelihood of a child receiving a later diagnosis of autism or another developmental or psychiatric condition, according to a study by U.S. researchers

Using records spanning a 19-year period at a women's hospital, Blake Gibson and colleagues identified 4,851 children born with placentas meeting criteria for placental inflammation (also called fetal inflammatory syndrome, or FIRS). In addition, they identified 31,927 controls born with normal placentas during the same period.

The researchers report that children born with placentas meeting criteria for FIRS were significantly more likely than controls to receive a diagnosis of autism spectrum disorder (ASD). In addition, they were more likely to be diagnosed with attention-deficit/hyperactivity disorder (ADHD), conduct disorder, or post-traumatic stress disorder (PTSD). The findings remained significant after adjusting for a variety of factors including a maternal history of psychiatric disorder or substance use and maternal prescriptions for anti-inflammatory drugs.

The researchers conclude, "This study has potential implications for clinical care and prevention approaches. Children born with placenta meeting criteria for FIRS should be monitored closely for early identification and treatment."

"Fetal inflammatory response and risk for psychiatric disorders," Blake Gibson, Eli Goodfriend, Yongqi Zhong, and Nadine M. Melhem, *Translational Psychiatry*, June 24, 2023 (free online). Address: Nadine M. Melhem, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, melhemnm@upmc.edu.

Vocal acoustics may offer a clue in diagnosing ASD

Researchers in France, Italy, and Chile report that differences in vocal acoustics (for instance, frequency and pitch) may be helpful in identifying children with autism spectrum disorders (ASD).

Frédéric Briend and colleagues compared 29 children with ASD to 20 typically developing (TD) children. In addition, they compared the group with ASD to 20 children with hearing loss who were fitted with cochlear implants, and to 15 children with developmental language disorder, because these conditions have commonalities with ASD.

Asking the children to repeat non-word sounds, the researchers measured nine different acoustic properties in their speech samples. They then used machine learning to develop an algorithm to classify the samples. They report, "We showed that voice acoustics classified autism diagnosis with an overall accuracy of 91 percent against TD children, and of 85 percent against a heterogeneous group of non-autistic children."

The researchers conclude, "Overall, our work suggests that easy-to-measure voice features, potentially linked to abnormal early neurodevelopment, can help in the diagnosis of autism spectrum disorder." While their study involved children who were around eight years of age, they say future research should investigate the acoustic cry features of babies as a potential biomarker for ASD.

"Voice acoustics allow classifying autism spectrum disorder with high accuracy," Frédéric Briend, Céline David, Silvia Silleresi, Joëlle Malvy, Sandrine Ferré, and Marianne Latinus, *Translational Psychiatry*, July 8, 2023 (free online). Address: Marianne Latinus, UMR 1253, iBrain, Université de Tours, INSERM, 37000 Tours, France, marianne.latinus@univ-tours.fr.

Use of epidural analgesia during delivery may raise likelihood of autism

A new large-scale study offers evidence that the use of labor epidural analgesia (LEA) during childbirth is associated with an elevated likelihood of autism spectrum disorders (ASD) in children.

Chunyuan Qiu and colleagues analyzed data on nearly 206,000 California children born by vaginal delivery between 2008 and 2017. They report, "Risk [for ASD] was approximately 20 percent greater with LEA exposure alone, compared with those unexposed after adjusting for multiple maternal, neonatal, and obstetric risk factors. Risk was 30 percent greater after exposure to both LEA and oxytocin compared with exposure to neither. However, we did not find significant ASD risk associated with oxytocin alone."

They conclude, "Our results call for more in-depth studies in varying study populations and practice to understand the complexity of labor and delivery and assess the long-term safety of a barrage of maternal medical interventions during labor and delivery, including LEA and oxytocin, on child health outcomes."

"Association of labor epidural analgesia, oxytocin exposure, and risk of autism spectrum disorders in children," Chunyuan Qiu, Sarah A.

Carter, Jane C. Lin, Jiaxiao M. Shi, Ting Chow, Vimal N. Desai, Vu T. Nguyen, Joseph Spitzer, R. Klara Feldman, and Anny H. Xiang, *JAMA Network Open*, July 21, 2023 (free online). Address: Chunyuan Qiu, Department of Anesthesiology, Kaiser Permanente Baldwin Park Medical Center, 1011 Baldwin Park Blvd, Baldwin Park, CA 91706, chunyuan.x.qiu@kp.org.

—and—
"Maternal labor epidural analgesia may be linked to autism in children," news release, Elana Gotkine, July 26, 2023.

High rate of vision problems seen in ASD

A new meta-analysis indicates that vision problems are common in individuals with autism spectrum disorders (ASD).

John Perna and colleagues analyzed data from multiple studies involving more than 15,000 people with ASD. They found that individuals with ASD had an increased prevalence of strabismus (improper eye alignment) and accommodation (focusing) deficits. In addition, they were more likely to have reduced peripheral vision, reduced stereoacuity (a measure of the ability of the eyes to work together), increased color discrimination difficulties, reduced contrast sensitivity, and increased retinal thickness.

The researchers conclude, "ASD is associated with some self-reported and objectively measured functional vision problems and structural alterations of the eye, even though we observed several methodological limitations in the individual studies included in our meta-analyses. Further research should clarify the causal relationship, if any, between ASD and problems of vision during early life."

"Association between autism spectrum disorder (ASD) and vision problems: A systematic review and meta-analysis," John Perna, Alessio Bellato, Preethi S. Ganapathy, Marco Solmi, Andrea Zampieri, Stephen V. Faraone, and Samuele Cortese, *Molecular Psychiatry*, July 26, 2023 (online). Address: Stephen Faraone, SVFaraone@upstate.edu.

Study Participants Sought

Dr. Lauren Moskowitz is seeking participants for a research study on the effectiveness of an online training program for parents of children with autism spectrum disorder (ASD) and co-occurring intellectual disability. The program is designed to help parents teach their children to overcome or cope with their fears or phobias. To learn more, contact Dr. Moskowitz at moskowl@stjohns.edu.

Age at diagnosis may not influence well-being of individuals with autism spectrum disorders

While a recent study reported that people who learned they were autistic at a young age fared better than individuals diagnosed at a later age (see ARRI 2022, No. 3), new research suggests that age at diagnosis may not correlate with a person's quality of life as an adult.

Florence Leung and colleagues asked 300 autistic adults to report the age at which they learned that they were autistic, as well as the age at which they received a diagnosis. In addition, participants provided information about their autistic traits, as well as data on a wide range of personal and demographic factors.

The researchers note that their study included a larger sample than the earlier study, and differentiated between the time when participants first learned that they were autistic and when they actually received an official diagnosis. In addition, the researchers analyzed many other factors contributing to overall quality of life, as well as exploring specific aspects of quality of life.

"Contrary to the previous study," they say, "we found the age at which one learns about their autism does not have a significantly independent impact on their quality of life as an adult. Rather, other factors (e.g., autistic traits, sex, and additional mental health conditions) may have a greater impact."

Leung says, "Our findings revealed that having more autistic personality characteristics—irrespective of when you learn you are autistic—was the strongest link to poor outcomes across all areas of quality of life." Additionally, the researchers found that autistic women reported a higher quality of life than autistic men, and people with additional mental health conditions such as anxiety reported a lower quality of life.

Study coauthor Lucy Livingston comments, "For some people, finding out they are autistic sooner rather than later was linked to a better quality of life. For others, finding out later was better. Overall, there was no overall link between the age they found out and their quality of life."

She adds, "There could be many reasons for this. Getting an autism diagnosis does not always lead to any meaningful additional support, so it could be that autistic people who learn they are autistic at an earlier age

did not necessarily experience a benefit to their life quality. Equally, a late diagnosis in adulthood can be a positive experience, helping people to make sense of themselves, which may improve their self-reported quality of life. The take-away message is that the impact of an autism diagnosis on someone's quality of life is different for everyone."

The researchers say, "Given our participant sample was larger and more diverse in age and education level compared to previous research, this finding is likely to be more applicable to autistic adults from different backgrounds." However, they say, "[We] are not suggesting that individuals should be made aware of their diagnosis later than sooner. Getting a timely diagnosis remains crucial for autistic people and their families to access appropriate support."

"Re-examining the association between the age of learning one is autistic and adult outcomes," Florence Y. N. Leung, Punit Shah, David

Mason, and Lucy A. Livingston, *Autism*, June 14, 2023 (free online). Address: Lucy Livingston, Department of Psychology, Institute of Psychiatry, Psychology & Neuroscience, King's College London, De Crespigny Park, London SE5 8AF, UK, lucy.livingston@kcl.ac.uk.

—and—
"Finding out you're autistic in later life can be a positive experience, say researchers," news release, Medical Xpress, June 15, 2023.

—www.Autism.Jobs—

A Free Resource for Job Seekers, Caregivers, Job Coaches, and Employers

At this site, you can discover the advantages of hiring individuals with autism, access practical information designed to help candidates with autism become "job ready," and learn how to create autism-friendly workplaces.

Older adults with ASD at higher risk for many health issues

A large-scale study from researchers in Sweden and Poland indicates that older adults with autism spectrum disorders (ASD) are at significantly higher risk than their non-autistic peers for a range of injuries and medical conditions.

Shengxin Liu and colleagues used two national registries in Sweden to study data on autistic and non-autistic individuals who were 45 years of age or older, excluding autistic individuals with chromosomal abnormalities. In all, their sample included more than 4 million adults, of whom 5,291 had a diagnosis of autism.

The researchers found that individuals with ASD had a higher risk of four of the five injuries they studied. Self-harm accounted for the greatest risk increase, followed by poisoning, falls, and other physical injuries.

Liu comments, "The risk of self-harm was worryingly high, a full seven times higher than in non-autistic people. Reasons behind this remain largely unknown. One possible contributing factor could be mental health conditions that commonly co-occur with autism, such as anxiety and depression."

The researchers also found that individuals with ASD had an increased risk for 15 of the 39 physical conditions they studied. For example, they had three times the risk for anemia and glucose dysregulation and nearly double the risk for heart failure, type 2 diabetes, and chronic obstructive pulmonary disease (COPD).

The researchers say that with some exceptions, the increased risks for individuals with ASD occurred equally in individuals with and without intellectual disability, and across both sexes. They stress that more investigation is needed to determine the causes for these increased risks. One possible contributing factor, they say, is that many of these individuals have a history of long-term psychotropic drug use, which can affect physical health.

They conclude, "Our findings highlight the urgent need to understand the underlying reasons for these health burdens, design targeted screening and intervention programs, and promote older care to enhance quality of life for older autistic people."

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"Age-related physical health of older autistic adults in Sweden: a longitudinal, retrospective, population-based cohort study," Shengxin Liu, Henrik Larsson, Ralf Kuja-Halkola, Paul Lichtenstein, Agnieszka Butwicka, and Mark J Taylor, *The Lancet Healthy Longevity*, June 6, 2023 (free online). Address: Shengxin Liu, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Solna 171 77, Sweden, shengxin.liu@ki.se.

—and—
"Autistic adults at substantial risk of injuries and age-related conditions, finds population-based study," news release, Karolinska Institutet, June 7, 2023.

WOMEN IN AUTISM

While autism was once viewed as a pediatric condition that nearly always affected boys, we now understand that autism is a lifelong neurodevelopmental condition with a diverse presentation across all genders. A new article on the Autism Research Institute's website describes the autism gender bias, explores real-world outcomes for autistic women, and discusses emerging research and new models for the future. You can read the article at:

autism.org/women-in-autism

Sensory-adapted dental offices lower stress of kids with ASD

Adapting dental offices for children with autism spectrum disorders (ASD) may make dental cleanings significantly less stressful for this population, according to a new study.

In a randomized crossover study led by Leah Stein Duker, 138 children with ASD underwent two dental cleanings, approximately six months apart. Half of the children initially underwent cleaning in a regular dental environment (RDE), and the other half in a sensory-adapted dental environment (SADE). At the second cleaning appointment, the two groups switched treatment modes.

The SADE condition used by the researchers was designed to address a wide range of sensory issues. “For the visual sensory domain,” the researchers say, “all overhead fluorescent lights and the dental operatory lamp were turned off and darkening curtains were applied to windows. A glasses-mounted headlight directed light into the child’s mouth (avoiding eyes), and slow-moving visual effects (i.e., bubbles or fish scenes chosen by the child or parent) were projected onto the ceiling in the child’s visual field. For the auditory sensory domain, a playlist of calming music (e.g., classical music with nature sounds) played in the room via a small speaker. Finally, for the tactile and deep pressure domain, a butterfly-shaped wrap weighted with a pediatric dental radiograph vest was used to apply deep tactile pressure stimuli to the child. The butterfly wrap fit around the dental chair, with the wings wrapping around the child from shoulders to ankles to provide a calming deep hug sensation.” Children could opt out of any of the sensory adaptations if they did not find them calming.

The researchers observed the children’s behavior during treatment and used finger electrodes to measure their electrodermal activity. They report that children exhibited significantly lower physiological stress during dental care in SADE compared with RDE. In addition, video analysis indicated that they exhibited a lower frequency and duration of behavioral distress in the SADE condition. The researchers also found that children’s physiological stress dropped as soon as they entered the SADE, before the cleaning even began, and that this initial level of physiological stress predicted behavioral distress during the cleaning. Younger children and those with a lower IQ or less expressive communication benefitted the most from the SADE setting.

“So many interventions try to change the person,” Stein Duker comments. “Instead, this intervention sees children for who they are—it does not try to fix or change them—focusing on the intervention to modify

problematic environmental factors as a way to empower the child and family to engage successfully in [the experience].”

Stein Duker says dental professionals and parents should work together to find ways to make the dental office less stressful for children with ASD or other children with sensory issues. She notes, “There are weighted X-ray bibs in every single dental office that may help calm the child; they can wear sunglasses; they can wear a beanie hat covering the ears to muffle noises—all of these are completely free and easy adaptations that have the potential to improve the clinic experience for those with sensory sensitivities, without negatively impacting dentists’ ability to provide care.”

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 “Sensory adaptations to improve physiological and behavioral distress during dental visits in autistic children: a randomized crossover trial,” Leah I. Stein Duker, Dominique H. Como, Caitlin Jollette, Cheryl Vigen, Cynthia L. Gong, Marian E. Williams, José C. Polido, Lucía I. Florindez-Cox, and Sharon A. Cermak, *JAMA Network Open*, June 2, 2023 (free online). Address: Leah I. Stein Duker, Division of Occupational Science & Occupational Therapy, University of Southern California, 1540 Alcazar St, CHP 133, Los Angeles, CA 90089, lstein@chan.usc.edu.

—and—
 “Sensory adapted dental rooms significantly reduce autistic children’s physiological stress during teeth cleanings,” news release, Mike McNulty, University of Southern California, June 1, 2023.

Quotable....

“Data show that autistic individuals have worse health outcomes not just as older adults, but also during childhood, adolescence, and early adulthood, with one study placing the average life expectancy of autistic individuals at just 39 years. Although autism alone does not reduce the lifespan, the fact that neurodivergent individuals can expect a lower life expectancy than do neurotypical people underlines the need for robust health systems, social support networks, and preventive strategies to preserve both health and quality of life for autistic individuals—particularly among geriatricians, who will often not have autism at the forefront of the clinical picture, but who will now be caring for older adults who were children at a time when a diagnosis of autism might easily have been missed.

“Even though the same cannot be said for all 11 cases in Kanner’s report, Donald Triplett’s history [see page 2] was, by his own account, a happy one: he went on to become a banker, a keen golfer, and to travel extensively by himself. Although his socioeconomic background undoubtedly played a part, if ‘autism’s first child’ could live a long and fulfilling life, there can be no reason for health and quality of life to elude any individual simply because of neurodiversity—no matter their age.”

Editorial, *The Lancet Healthy Longevity*, July 2023

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Conducting and sponsoring research on the causes of and best treatments for autism (more than \$475,000 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.

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