

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

Prenatal ultrasounds may point to children at higher risk of developing autism

Routine prenatal ultrasounds may be able to reveal an increased risk for autism spectrum disorder (ASD), according to a new study from Israel.

Ohad Regev and colleagues analyzed fetal ultrasound data from 659 children. Of the group, 229 had ASD, 201 were closest-in-age siblings of the children with ASD, and 229 were neurotypical controls.

The researchers detected anomalies—primarily of the heart, urinary system, brain, and head—in 30 percent of unborn children who later developed ASD, a rate twice as high as that seen in non-ASD siblings and three times as high as that seen in the neuro-

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typical controls. Anomalies occurred more often in girls than in boys, and the severity of the anomalies correlated with the subsequent severity of ASD.

Study coauthor Idan Menashe says, “Previous studies have shown that children born with congenital diseases, primarily those involving the heart and kidneys, had a higher chance of developing ASD. Our findings suggest that certain types of ASD that involve other organ anomalies begin and can be detected in utero.” Menashe believes doctors may be able to use prenatal ultrasounds to evaluate the probability of a child being born with ASD, allowing for very early treatment.

“Association between ultrasonography foetal anomalies and autism spectrum disorder,” Ohad Regev, Amnon Hadar, Gal Meiri, Hagit Flusser, Analya Michaelovski, Ilan Dinstein, Reli Hershkovitz, and Idan Menashe, *Brain*, January 17, 2022 (online). Address: Idan Menashe, Department of Public Health, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva 8410501, Israel, idanmen@bgu.ac.il.

—and—

“Routine prenatal ultrasound can identify early signs of autism,” news release, Ben-Gurion University of the Negev, February 9, 2022.

Maternal sleep apnea may cause autism-like changes in males

A new animal study suggests that maternal sleep apnea during pregnancy may increase the risk of male children developing brain and behavioral changes associated with autism.

Amanda Vanderplow and colleagues note, “Sleep apnea is characterized by recurrent partial or complete cessation of breathing during sleep, often hundreds of times each night. The resulting swings in blood oxygen levels (intermittent hypoxia) induce profound inflammation, which causes most of the morbidities associated with sleep apnea.” The researchers note that by the third trimester, sleep apnea occurs in about 15 percent of uncomplicated pregnancies and more than 60 percent of high-risk pregnancies.

To determine if maternal sleep apnea might affect the development of children, the researchers subjected pregnant rats to intermittent low oxygen levels at times of rest during the second half of pregnancy. As expected, the intervention led to hypoxia in the mothers, but not in the fetuses.

The researchers report that the offspring of rats exposed to intermittent hypoxia exhibited an increased incidence of cognitive and executive function impairment. (Executive function refers to higher-level brain

functions such as planning and impulse control.) In addition, the affected offspring exhibited abnormal juvenile communicative vocalizations, altered social behavior, and increased grooming behavior (a form of repetitive behavior). With the exception of abnormal vocalizations, behavioral alterations occurred solely in male and not female offspring.

As well as behavioral changes, the affected offspring exhibited significant abnormalities in the density and structure of dendritic spines, which are the protrusions on neurons that receive and integrate signals from other neurons. While adolescent rats of both sexes showed an elevated density of dendritic spines, the increase was much more marked in males. This increase, the researchers say, was due primarily to a lack of spine “pruning,” which is critical for normal brain development.

In addition, the researchers found that affected offspring exhibited excess activity of a cell signaling pathway called the mTOR pathway. Studies have shown that this pathway is altered in autism. Administration of rapamycin, an mTOR inhibitor, partially mitigated the behavioral effects of maternal hypoxia.

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Anxiety in children with ASD linked to differences in amygdala

Changes in the amygdala—an almond-shaped region in the brain—appear to be linked to the development of anxiety in children with autism spectrum disorders (ASD), according to a new study.

Anxiety is one of the most common comorbidities in autism, with research indicating that 69 percent of children with ASD suffer from anxiety compared to only 8 percent of non-autistic children. Research indicates that dysregulation of the amygdala plays a role in anxiety, and that the growth trajectory of the amygdala is altered in many individuals with ASD.

In the new study, Derek Sayre Andrews and colleagues used magnetic resonance imaging (MRI) to scan the brains of 71 children with ASD and 55 non-autistic controls as many as four different times when the chil-

dren were between 2 and 12 years of age. The researchers also interviewed parents when the children were between 9 and 12 years of age to determine the children’s levels of traditional or autism-distinct anxiety.

The researchers explain that the two types of anxiety are similar, but the latter involves anxiety arising within an autistic context. For instance, they say, autism-distinct anxiety may involve fears related to social confusion (as opposed to fear of negative evaluation), uncommon phobias (for instance, a fear of specific sounds or certain facial features), excessive worry related to losing access to materials related to circumscribed interests, or fears of change.

The researchers found that nearly half of the children with ASD exhibited traditional

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Low levels of protein in CSF linked to autism and epilepsy

Low levels of a “calming” brain protein may play a key role in autism and epilepsy, according to a new study.

M. Dolores Martin-de-Saavedra and colleagues measured levels of a protein called CNTNAP2 in the cerebrospinal fluid (CSF) of individuals with autism as well as neurotypical controls. The researchers found that individuals with autism had fewer molecules of CNTNAP2 floating freely in the CSF.

CNTNAP2 is best known for being a cellular adhesion protein that helps neurons connect to one another. However, the researchers say that when CNTNAP2 is floating freely, it functions more like a hormone than a cellular glue, binding to neurons and reducing excitatory neurotransmissions. Therefore, they say, CNTNAP2 may play a role as a regulator of excitatory activity.

“When the brain is getting too excited, CNTNAP2 gets broken off and attaches to brain cells as a sort of feedback switch,” study coauthor Peter Penzes says. “If you don’t have CNTNAP2, there’s hyper-connectivity between neurons which can contribute to autism, and there’s excessive excitation of neurons which can lead to seizures.”

The researchers say their study helps to establish a link between autism and epilepsy, two conditions that frequently co-occur. Additionally, they say, their findings could lead to treatments for individuals with autism and comorbid epilepsy.

“Shed CNTNAP2 ectodomain is detectable in CSF and regulates Ca²⁺ homeostasis and

network synchrony via PMCA2/ATP2B2,” M. Dolores Martín-de-Saavedra, Marc Dos Santos, Lorenza Culotta, Olga Varea, Benjamin P. Spielman, Euan Parnell, Marc P. Forrest, Ruoqi Gao, Sehyoun Yoon, Emmarose McCoig, Hiba A. Jalloul, Kristoffer Myczek, Natalia Khalatyan, Elizabeth A. Hall, Liam S. Turk, Antonio Sanz-Clemente, Davide Comoletti, Stefan F. Lichtenhaler, Jeffrey S. Burgdorf, Maria V. Barbolina, Jeffrey N. Savas, and Peter Penzes, *Neuron*, December 19, 2021 (online). Address: Peter Penzes, p-penzes@northwestern.edu.

—and—

“New autism biomarker discovered in cerebrospinal fluid,” news release, Will Doss, Northwestern University, December 17, 2021.

Anxiety in ASD linked to differences in amygdala

(continued from page 1)

anxiety, autism-specific anxiety, or both. Those with traditional anxiety had significantly larger right amygdala volumes compared to controls, but the developmental trajectory of the amygdala was similar for both groups. In contrast, they say, children with autism-distinct anxiety “had slower development of the right amygdala from the ages of around 3 to 11 compared to typically developing and other autistic children, and smaller right amygdala volumes at around 11 years of age compared to other autistic children.”

Study coauthor Christine Wu Nordahl says, “We were reminded that different autistic subgroups may have different underlying brain changes. If we had lumped both traditional and distinct anxieties together, the amygdala changes would have canceled each other out and we would not have detected these different patterns of amygdala development.”

The researchers caution that their study sample was fairly small, and in particular contained few females with ASD. In addition, they note, their focus was limited to the amygdala, which has broad connections to many other brain regions whose role in anxiety in ASD needs to be explored.

“Association of amygdala development with different forms of anxiety in autism spectrum disorder,” Derek Sayre Andrews, Leon Akshman, Connor M. Kerns, Joshua K. Lee, Breanna M. Winder-Patel, Danielle Jenine Harvey, Einat Waizbard-Bartov, Brianna Heath, Marjorie Solomon, Sally J. Rogers, Andre Altmann, Christine Wu Nordahl, and David G. Amaral, *Biological Psychiatry*, February 2022 (online). Address: Derek Sayre Andrews, 2825 50th St, Sacramento CA 95817, dandrews@ucdavis.edu.

—and—

“Amygdala changes in autistic individuals linked to anxiety,” news release, UC Davis, February 10, 2022.

Autistic traits common in teens, young adults with a substance use disorder

Many teens and young adults who seek treatment for a substance use disorder (SUD) exhibit previously unidentified traits characteristic of autism spectrum disorder (ASD), according to a new study.

James McKowen and colleagues asked parents of 69 adolescents or young adults who were visiting an SUD clinic for the first time to evaluate their children using the Social Responsiveness Scale-2 (SRS-2). This form is designed to measure social awareness, social cognition (thinking about other people and interactions with them), social communication, social motivation, and restricted interests and repetitive behaviors. It has been shown to reliably identify the presence and severity of social impairment in individuals with ASD, and to distinguish autism from other disorders.

“Usually, studies of substance use disorder in autism are done in those with an autism diagnosis already,” McKowen says. “We have looked at this question from the other side, asking how many people with substance use disorder have autism.”

The researchers found that 20% of the teens and young adults had elevated scores on the SRS-2. They say the findings highlight the importance of assessing patients in an SUD treatment setting for autistic traits.

For parents of children with an SUD, McKowen adds, “the big takeaway is that if you suspect that your child may have an autism spectrum issue or if school personnel have suggested that your child may have autistic traits, you should certainly get that assessed, and let your clinicians know whether your child has had a prior diagnosis of ASD.”

“Characterizing autistic traits in treatment-seeking young adults with substance use disorders,” James McKowen, Diana Woodward, Amy M. Yule, Maura DiSalvo, Vinod Rao, Julia Greenbaum, Gagan Joshi, and Timothy E. Wilens, *American Journal on Addictions*, December 2021 (online). Address: James McKowen, Clinical and Research Programs in Pediatric Psychopharmacology and Adult ADHD, Massachusetts General Hospital, 15 Parkman St., Wang Bldg., Suite 805, Boston, MA 02114, jmkowen@mgh.harvard.edu.

—and—

“Undiagnosed autistic traits common among youths with substance use disorders, study finds,” news release, Massachusetts General Hospital, January 24, 2022.

Free Webinars

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EDITORIAL: Stephen M. Edelson, Ph.D.

Planning for the future of autism research

As a result of the slowdown in autism research over the past two years due to the pandemic, we have an opportunity to reevaluate our current understanding of autism and decide where we want to go in the future. This is our chance to construct a roadmap that will allow us to reach two crucial goals: completing our understanding of autism, and determining how best to help individuals on the autism spectrum. But to create this roadmap, we will need to change the status quo.

Moving from the past to the future: Why we need an “end game”

Over the past decades—beginning with the revolutionary work of Dr. Bernard Rimland—the history of autism research has been one of temporary leaps forward, followed by periods where little or no progress has been made.

Before the 1960s, there was little real research into autism. Most clinicians had accepted the prevailing theory that “refrigerator mothers” caused autism, despite the absence of any evidence for this. In 1964, Dr. Rimland turned the entire autism field topsy-turvy by arguing, based on previously published research as well as clinical and parent reports, that autism was the result of an underlying biological condition as opposed to parental emotional neglect.

This new paradigm galvanized the autism research field, and soon afterward, acclaimed research centers in Los Angeles, New York, and London began publishing papers. Researchers initially focused their attention on genetics, neurology, and challenging behaviors. However, over the next five decades, their focus expanded to include metabolism, immunology, and the gastrointestinal system in addition to anxiety, cognition, sensory processing, sleep disturbances, and social interaction.

Unfortunately, with few exceptions, all of these fields have remained independent from one another. This lack of a coordinated plan has led to dead ends, U-turns, and even reckless directions.

Rather than coordinating its efforts, the autism community seems to be waiting for a point in time when a single incredible finding solves all of the riddles of autism, or when all of the findings will magically interconnect with one another to form a complete picture. We have waited far too many years for this miraculous moment in time. Because of this, only a handful of evidence-based treatments are currently available to help individuals with autism spectrum dis-

orders (ASD). Sadly, this has led to a less than optimal quality of life for most of these individuals.

What the autism research community needs now is a strategy for reaching an endgame. In other words, we need a coordinated plan for moving research forward in a manner that will produce real results in the near future—results that will make a true difference in the lives of individuals with ASD and their families.

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The basics of a strategic plan

A strategic plan does not need to be complex. Its goal could be as straightforward as “to understand the autism spectrum and determine a standard of care.”

A strategic plan for autism research should address individuals from childhood through old age, on every part of the autism spectrum. Furthermore, it should include realistic goals and practical timelines, be they 20, 30, or possibly 50 years from now. If we do not establish such goals and timelines, research on autism could continue well into the next century without making significant progress.

Rather than “reinventing the wheel,” a strategic plan could be based on issues already identified by two respected groups:

- The *Lancet*, an internationally renowned journal, recently published a well-received committee report on the future of autism research and care. The report described the numerous known needs of the autism community and offered various solutions, such as offering early intervention, understanding how interventions work, and providing better access to services for underserved populations.
- The Interagency Autism Coordination Committee (IACC) is a federal advisory committee that coordinates federal efforts and provides advice to the Secretary of Health and Human Services on issues related to ASD. It includes both federal and public members. IACC committee members encourage funding

for numerous areas of research, such as the early detection, underlying biology, and treatment of autism. The IACC also monitors support from government and private organizations on these issues. Unfortunately, they do not track or publish summaries of these research findings.

A strategic plan should include a program to carefully monitor all published findings. Tracking all research is important since the relatedness of findings, either directly or indirectly, may not be obvious until future studies fill in the gaps in our understanding of autism. In addition, a monitoring program would help us make sense of the numerous inconsistent findings that have plagued autism research from the get-go.

The goals of a strategic plan should not be chosen by a handful of agencies and organizations, but rather should be agreed upon by representatives of all stakeholders in the autism community. This could be done with a vote. Given today’s technology, such a vote would be challenging but certainly possible—and it would help to ensure that all members of the community were on board.

Lastly, all representatives should agree, in principle, to work collaboratively and acknowledge that negotiation is the only way for the plan to succeed. Progress will not occur if we remain in individual silos or, worse yet, warring camps.

When do we start—and how?

The answer to the first part of this question is simple: We should start now. The more quickly we create a strategic plan, the faster we can find the answers to our questions about autism, and the more quickly individuals with ASD will begin to benefit from our work.

As to how we start, I believe we should look to the example of Dr. Rimland, a parent who single-handedly changed the world of autistic individuals for the better. He showed us that one dedicated and very motivated person, family, or organization can be enough to ignite a rally within the autism community.

The Autism Research Institute encourages active members of the autism community to work together to develop and implement a strategic plan. The sooner the better! Let’s stop sitting back and waiting for an elusive “magic moment,” and start actively planning a highway to the future.

Research Updates

Some antipsychotic drugs may hike breast cancer risk

Antipsychotic medications are frequently prescribed for women with autism, but new research suggests that some of these drugs may significantly increase a woman's risk for breast cancer.

Noting that a number of antipsychotic drugs increase levels of the hormone prolactin—which can lead to menstrual cycle irregularities, abnormal breast milk production, and abnormal breast tissue growth—Tahir Rahman and colleagues investigated the possibility that these drugs might affect women's risk for breast cancer as well. The researchers used data collected from 2012 through 2016 on 540,737 women between the ages of 18 and 64 who took antipsychotics. They investigated three categories of antipsychotic medications:

- Drugs associated with high prolactin levels, such as haloperidol, paliperidone, and risperidone.
- Drugs with “mid-range” effects on prolactin, including iloperidone, lurasidone, and olanzapine.
- Drugs with a smaller effect on prolactin levels, such as aripiprazole, asenapine, brexpiprazole, cariprazine, clozapine, quetiapine, and ziprasidone.

The researchers compared the effects of all three categories of antipsychotic drugs to the effects of anticonvulsant drugs and lithium, which also are often prescribed to treat psychiatric disorders. When compared with these types of drugs, the relative risk of breast cancer was 62% higher for women who took antipsychotic drugs associated with high levels of prolactin and 54% higher for those taking antipsychotic drugs with “mid-range” effects. Antipsychotics that had little effect on prolactin were not associated with any increase in breast cancer risk.

Rahman says, “Our study confirms findings from a smaller European study that advised women and their doctors to first try drugs that don't affect prolactin levels. We agree with that advice and believe psychiatrists should start to monitor prolactin levels in their patients taking antipsychotics.”

Editor's note: Since antipsychotics can cause enlargement of the breast tissue in men (gynecomastia), it is possible that these drugs may also increase males' risk for breast cancer. This issue needs to be examined.

“Risk of breast cancer with prolactin elevating antipsychotic drugs: An observational study of US women (ages 18-64 years),” Tahir Rahman, John M. Sahrman, Margaret A. Olsen, Katelin B. Nickel, J. Phillip Miller, Cynthia Ma, and Richard A. Gruzza, *Journal of Clinical Psycho-*

pharmacology, December 3, 2021 (online). Address: Tahir Rahman, Department of Psychiatry, Washington University in St. Louis, 660 S Euclid Ave, Campus Box 8134, St. Louis, MO 63110, trahman@wustl.edu.

—and—

“Antipsychotic drugs may increase risk of breast cancer,” news release, Washington University School of Medicine in St. Louis, December 9, 2021.

School closures strongly impact children with ASD

Data from a recent survey indicate that children with autism spectrum disorders (ASD) have been more severely impacted than neurotypical children by school shutdowns during the COVID-19 pandemic.

Helen Genova and colleagues surveyed 250 parents of children between 4 and 15 years of age. Two-thirds of the children were neurotypical, while one-third had ASD.

The researchers report, “Overall, parents of children with autism were more than three times as likely to report negative changes in their child compared to parents of neurotypical children. When asked about autism-specific stressors, parents of autistic children reported concerns related to hygiene, behavioral regression, therapy disruption, meltdowns, and returning to school.” While neurotypical children suffered primarily as a result of isolation from their peers, children with ASD struggled most with routine disruptions. The researchers also found that children with ASD participated less than neurotypical children in virtual social experiences, putting them at even greater risk of negative outcomes.

“While returning to school and socialization may represent a panacea for neurotypical children,” the researchers conclude, “it is possible that children with autism may have significant needs resulting from the pandemic that must be examined. For example, educational losses (due to inability to attend to an online format), must be directly addressed in order for children with autism to ‘catch up’ to their peers. It would be unacceptable for an entire generation of autistic children to continue to struggle with educational goals compared to their peers.”

“Effects of school closures resulting from COVID-19 in autistic and neurotypical children,” Helen M. Genova, Aditi Arora, and Amanda L. Botticello, *Frontiers in Education*, November 23, 2021 (free online). Address: Helen Genova, hgenova@kesslerfoundation.org.

—and—

“Survey heightens concern about pandemic's impact on education of students with autism,” news release, Kessler Foundation, February 17, 2022.

Transportation issues rarely addressed by providers

Very few medical or behavioral specialists discuss driving or other transportation-related issues with patients who have ASD (autism spectrum disorders), according to a new study.

Emma Sartin and colleagues surveyed 78 providers, mostly pediatric physicians and psychologists who care for both autistic and non-autistic patients. Half of the providers reported having transportation-related discussions with non-autistic patients, while only one in five discussed transportation issues with patients with ASD. A third of providers believed they were able to assess if non-autistic patients were capable of driving, while only 8 percent believed they could assess the readiness of patients with ASD.

The researchers say helping individuals with ASD to navigate transportation issues is important because the ability to travel, whether by driving or by using public transportation, improves psychosocial, health, and employment outcomes. They also note that newly licensed young autistic drivers have similar or lower crash rates compared to non-autistic peers, and that young drivers with ASD are much less likely to have their licenses suspended or to receive a traffic violation than their non-autistic peers.

They conclude, “There is a critical need to develop resources for use in medical settings to effectively support autistic adolescents' independence and mobility as they transition into adulthood.”

Study coauthor Benjamin Yerys adds, “One important way that providers can help autistic teens and their families is to start talking about driving and transportation before they get to high school. We know this seems early, but it provides more time for them to benefit from supports, including those services that come from outside of healthcare, including tailored instruction from a driving rehabilitation specialist.”

“Brief report: healthcare providers' discussions regarding transportation and driving with autistic and non-autistic patients,” Emma B. Sartin, Rachel K. Myers, Christina G. Labows, Kristina B. Metzger, Meghan E. Carey, Benjamin E. Yerys, Catherine C. McDonald, Cynthia J. Mollen, and Allison E. Curry, *Journal of Autism and Developmental Disorders*, December 2021 (online). Address: Emma B. Sartin, Center for Injury Research and Prevention, Children's Hospital of Philadelphia, 2716 South Street, Philadelphia, PA 19146, sartine@chop.edu.

—and—

“Study finds few pediatric providers discuss transportation with their autistic patients,” news release, Children's Hospital of Philadelphia, December 16, 2021.

Research Updates

Average or high IQ in individuals with ASD may be higher than previously estimated

The number of individuals who have autism spectrum disorders (ASD) without intellectual impairment is higher than previously believed, according to recent research.

Maja Katusic and colleagues examined the medical and school records of more than 30,000 individuals born between 1976 and 2000 in Olmsted County, Minnesota. They identified cases of ASD based on behavioral data in the records, using both broad and narrow definitions of autism as defined by the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). In addition, they identified individuals with documented clinical autism diagnoses.

The researchers found that of 890 individuals who met the inclusive definition of autism and had IQ scores available, 59 percent had an average or higher IQ score. Of the 453 individuals who met the narrow criteria, 51 percent had an average or higher IQ score. Only 43 percent of the 187 individuals with a clinical diagnosis of ASD had an average or higher IQ score. Males were more likely than females to have average or higher IQs.

The researchers say their findings “suggest that nearly half of individuals with ASD have average or higher IQ,” and warn that these individuals “remain at risk for not being identified.”

“IQ in autism spectrum disorder: a population-based birth cohort study,” Maja Z. Katusic, Scott M. Myers, Amy L. Weaver, and Robert G. Voigt, *Pediatrics*, November 4, 2021 (online ahead of print publication). Address: Maja Katusic, Mayo Clinic, 200 1st St SW Rochester, MN 55902, katusic.maja@mayo.edu.

“Autism without intellectual impairments more common than previously reported,” Jonathan Moens, *Spectrum News*, December 1, 2021.

Cochlear implants may benefit some children with comorbid ASD, deafness

Some children with autism spectrum disorders (ASD) who are also deaf may benefit significantly from receiving a cochlear implant, according to a new study.

A cochlear implant is an electronic device that restores partial hearing. The device uses a sound processor located behind the ear to capture sound signals, sending them to an implanted receiver that forwards them

to electrodes implanted in the cochlea. The signals stimulate the auditory nerve, which then directs the signals to the brain.

Carolyn Jenks and colleagues investigated the outcomes of 30 children with ASD who received cochlear implants between 1991 and 2018. At the time of implantation, recipients ranged in age from infancy to 11 years of age. At follow-up, 73 percent of recipients used their implants consistently throughout the day.

The researchers report that 33 percent of all users, and 45 percent of consistent users, developed measurable speech perception ability by an average of 4.5 years of use. “Spoken language alone was used by 31 percent and spoken plus sign by 14 percent,” they say, “with the remainder using sign alone, augmentative communication devices, or no mode of communication.”

The researchers add that according to parent reports, 86 percent of cochlear implant recipients showed improvements in social engagement. The behaviors parents reported most frequently as improved were communication and attention.

They conclude, “Findings support a growing body of literature that cochlear implantation has the potential to improve auditory skills [and] language and enhance social engagement in some deaf children with autism spectrum disorder.”

“Cochlear implantation can improve auditory skills, language and social engagement of children with autism spectrum disorder,” Carolyn M. Jenks, Stephen R. Hoff, Jennifer Haney, Elizabeth Tournis, Denise Thomas, and Nancy M. Young, *Otology & Neurotology*, December 2021 (online). Address: Nancy Young, Ann & Robert H. Lurie Children’s Hospital of Chicago, Division of Pediatric Otolaryngology, Section of Otolaryngology and Neurotology, 225 East Chicago Ave., Box #25, Chicago, I 60611, nyoung@luriechildrens.org.

“Cochlear implant in deaf children with autism can improve language skills and social engagement,” news release, Ann & Robert H. Lurie Children’s Hospital of Chicago, December 23, 2021.

EMDR Study

The Johnson Center for Child Health and Development is conducting a study of Eye Movement Desensitization and Reprocessing (EMDR) for addressing anxiety and post-traumatic stress. Participants will be ages 18 or older, have an autism diagnosis, and have experienced traumatic or adverse events. Participants must be within traveling distance of the research location in Austin, TX.

For more information, call (512)732-8400 or email info@johnson-center.org.

Study suggests association between inflammation, GI problems in kids with ASD

A new study by researchers in Egypt offers evidence that inflammation plays a role in the gastrointestinal (GI) problems common in children with autism spectrum disorders (ASD).

Hanan Galal Azouz and colleagues assessed fecal levels of a protein called calprotectin in 40 children with ASD and 40 controls. Elevated levels of fecal calprotectin (FC) are considered a marker for GI inflammation. In addition, the researchers rated the severity of autism in the ASD group using the Childhood Autism Rating Scale (CARS) and assessed their GI symptoms using a modified six-question version of the Gastrointestinal Severity Index (6-GSI).

They report that 82.5 percent of children with ASD exhibited GI symptoms, and 35 percent had high scores on the 6-GSI. FC levels were elevated in 35 percent of individuals with ASD compared to 25 percent of controls, and mean FC levels were significantly higher in children with ASD compared to controls. The researchers found positive correlations between CARS scores and GI severity scores as well as between FC levels and GI severity scores, although there was no significant correlation between CARS scores and FC levels.

They conclude, “FC as a lab marker and GI severity score could be utilized as an indicator of GI problem severity in autistic patients with GI symptoms.”

“Gastrointestinal manifestations and their relation to faecal calprotectin in children with autism,” Hanan Galal Azouz, Nermine Hosam El-din Zakaria, Ahmed Fouad Khalil, Sara Mohammad Naguib, and Mona Khalil, *Gastroenterology Review (Przegląd Gastroenterologiczny)*, December 2, 2021 (online). Address: Mona Khalil, Department of Paediatrics, Faculty of Medicine, Alexandria University, Alexandria, Egypt, drmonakhalil@yahoo.com.

ARI Survey: Seniors with Autism Spectrum Disorder

https://www.autism.org/adult_survey

If you or a person you care for is on the autism spectrum and is 50 years of age or older, we would appreciate it if you could complete this online form.

We hope the results from this survey will provide insight into the needs and challenges faced by seniors with autism and their support providers.

Study explores the neural roots of different responses to “motherese” by neurotypical children and children with ASD

Most very young children prefer “motherese”—the simplified, exaggerated, melodic speech that mothers typically use to talk to infants and toddlers—over regular speech. However, children with autism spectrum disorders (ASD) tend to show a reduced preference for motherese.

In a new study, Yaqiong Xiao and colleagues investigated the reasons for this difference. The researchers evaluated 71 toddlers and 14 adults with and without ASD, using three approaches:

- Functional magnetic resonance imaging (fMRI) scans performed while the children were asleep, to measure brain responses to motherese and other forms of social affective speech.
- Clinical assessments of social and language development.
- Eye tracking, to measure responses to females speaking motherese versus non-speech computer sounds and images.

The researchers found that individual differences in early social and language development correlated with responses in the superior temporal cortex—a brain region that processes sound and language—to motherese. Autistic infants and toddlers with the poorest neural responses to motherese also displayed the most severe social symptoms, poorest language outcomes, and greatest impairment of behavioral preference and attention toward motherese. Conversely, typically developing infants and toddlers showed the strongest neural responses and affinity to motherese. The researchers used a tool called “similarity network fusion” to correlate eye-gaze patterns to neural and behavioral responses, offering further support for their findings.

“We conclude,” the researchers say, “that significantly reduced behavioral preference for motherese in autism is related to impaired development of temporal cortical

systems that normally respond to parental affective speech.”

Study coauthor Karen Pierce adds, “The fact that a few children with autism did show strong brain activation and good attention to motherese speech is encouraging for two reasons: First, because it suggests that these particular toddlers with autism are likely to have good outcomes, a newly discovered and important subgroup. And second, it suggests a novel avenue for treatment.”

“Neural responses to affective speech, including motherese, map onto clinical and social eye tracking profiles in toddlers with ASD,” Yaqiong Xiao, Teresa H. Wen, Lauren Kupis, Lisa T. Eyster, Disha Goel, Keith Vaux, Michael V. Lombardo, Nathan E. Lewis, Karen Pierce, and Eric Courchesne, *Nature Human Behavior*, January 3, 2022 (online). Address: Yaqiong Xiao, Autism Center of Excellence, Department of Neurosciences, University of California San Diego, La Jolla, CA 92093, yaq.xiao@gmail.com.

“When mom talks, are infants with ASD listening?”, news release, University of California San Diego, January 3, 2022.

Sleep apnea effects studied (continued from page 1)

Study coauthor Michael Cahill says, “To our knowledge, this is the first direct demonstration of the effects of maternal intermittent hypoxia during gestation on the cognitive and behavioral phenotypes of offspring. Our data provide clear evidence that maternal sleep apnea may be an important risk factor for the development of neurodevelopmental disorders, particularly in male offspring.”

“A feature of maternal sleep apnea during gestation causes autism-relevant neuronal and behavioral phenotypes in offspring,” Amanda M. Vanderplow, Bailey A. Kermath, Cassandra R. Bernhardt, Kimberly T. Gums, Erin N. Seablom, Abigail B. Radcliff, Andrea C. Ewald, Mathew V. Jones, Tracy L. Baker, Jyoti J. Watters, and Michael E. Cahill, *PLOS Biology*, February 2, 2022 (free online). Address: Michael Cahill, Department of Comparative Biosciences, University of Wisconsin-Madison, Madison, Wisconsin 53706 michael.cahill@wisc.edu.

“Mothers’ sleep apnea may increase risk of autism-like changes in their male offspring,” news release, Public Library of Science, February 3, 2022.

Transcranial direct current stimulation of the cerebellum may have significant benefits for some children with ASD

A new study indicates that transcranial direct current stimulation (tDCS) applied to the cerebellum may significantly benefit some individuals with autism spectrum disorders (ASD).

The open-label pilot study, conducted by Giordano D’Urso and colleagues, involved seven children with ASD, all between 9 and 13 years of age, who underwent 20 daily sessions of tDCS applied to the right cerebellar lobe of the brain. tDCS involves the application of a weak electrical current to a specific area of the brain—in this case, the cerebellum—via one or more electrodes placed on the scalp.

“At the end of the treatment,” the researchers say, “the Aberrant Behavior Checklist (ABC) scores showed a 25% mean reduction in global severity of symptoms, with a more pronounced reduction in the ‘social withdrawal and lethargy’ (–35%), ‘hyperactivity and noncompliance’ (–26%), and ‘irritability, agitation, and crying’ (–25%) subscales.” In addition, parents reported significant improvements in their children’s sleep. Little improvement was seen in stereotypic behaviors and none in inappropriate speech, and no significant improvements were seen in two children who were taking psychotropic drugs.

The researchers say the intervention appeared to markedly reduce the severity of

tics in one child with a comorbid tic disorder, and to lead to the disappearance of a frontal epileptogenic focus in another child with a history of seizures. They add that it was generally accepted by patients and well tolerated, with no serious adverse events seen.

The researchers conclude that “cerebellar tDCS is safe, feasible, and potentially effective in the treatment of ASD symptoms among children.” However, they note that their study had a small sample size, an open-label design, and a short-term follow-up, and that their findings need to be confirmed by larger studies.

“Cerebellar transcranial direct current stimulation in children with autism spectrum disorder: a pilot study on efficacy, feasibility, safety, and unexpected outcomes in tic disorder and epilepsy,” Giordano D’Urso, Elena Toscano, Veronica Sanges, Anne Sauvaget, Christine E. Sheffer, Maria Pia Riccio, Roberta Ferrucci, Felice Iasevoli, Alberto Priori, Carmela Bravaccio, and Andrea de Bartolomeis, *Journal of Clinical Medicine*, January 2022 (free online). Address: Giordano D’Urso, giordanodurso@gmail.com.

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

This database is a searchable collection of autism employment resources with a wealth of practical advice. It includes links to a variety of resources including articles, videos, books and more.

Visit <https://www.autism.org/employment-resources-for-individuals-with-autism>

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Study hints at involvement of GABA in ASD sensory issues

Individuals with autism spectrum disorders (ASD) often exhibit anomalies in visual processing, and a new study indicates that alterations in the activity of the neurotransmitter GABA may play a role in these issues.

Qiyun Huang and colleagues analyzed electroencephalogram (EEG) recordings

Huang says, “What we have in this study is the first direct evidence that a specific visual response in the human brain is regulated by GABA, but quite differently in neurotypical and neurodiverse individuals.”

from 44 adults, 19 of whom had ASD. The researchers focused on the activity of the occipital lobe—the region of the brain that processes vision—in response to a series of visual stimuli with high and low contrast. EEGs were performed with and without the administration of a drug called arbaclofen, which switches on GABA type B receptors.

The researchers found that for non-autistic adults, 30 milligrams of arbaclofen disrupted visual processing. In individuals with ASD, however, the same dose of arbaclofen caused visual processing to become more like that of the non-autistic group at baseline.

Huang says, “We have known for some time that the GABA pathways in the brain might play a role in the way autistic people process visual information and the behaviors that rely on this information. What we have in this study is the first direct evidence that a specific visual response in the human brain is regulated by GABA, but quite differently in neurotypical and neurodiverse individuals.”

The researchers say their findings, while preliminary, suggest that arbaclofen may help to alleviate visual symptoms in individuals with ASD.

“GABA_B receptor modulation of visual sensory processing in adults with and without autism spectrum disorder,” Qiyun Huang, Andreia C. Pereira, Hester Velthuis, Nichol M. L. Wong, Claire L. Ellis, Francesca M. Ponteduro, Mihail Dimitrov, Lukasz Kowalewski, David J. Lythgoe, Diana Rotaru, Richard A. E. Edden, Alison Leonard, Glynis Ivin, Jumana Ahmad, Charlotte M. Pretzsch, Eileen Daly, Declan G. M. Murphy, and Grainne M. McAlonan, *Science Translational Medicine*, Vol. 14, No. 626, January 5, 2022 (online). Address: Grainne M. McAlonan, grainne.mcalonan@kcl.ac.uk.

—and—

“New study demonstrates link between brain chemical and visual processing in autism,” news release, King’s College London, January 5, 2022.

Impairments in interoception seen in children with ASD

Researchers in China report that children with autism spectrum disorders (ASD) exhibit impairments in interoception, which is the ability to process and integrate internal signals such as heartbeat and breathing patterns.

Han-xue Yang and colleagues evaluated 30 children with ASD, 20 children with comorbid ASD and attention-deficit/hyperactivity disorders (ADHD), and 63 neurotypical controls, using an eye-tracking interoceptive accuracy test (EIAT). The neurotypical controls were further divided into those with and without elevated levels of autism traits.

The EIAT shows two bouncing rabbits on a screen, and participants are asked to look at the shape that is bouncing in synchrony with their heartbeats. An eye tracker captures their eye movements, while a pulse oximeter measures their heart rates in real time.

The researchers report that autistic children either with or without ADHD exhibited lower interoceptive accuracy on the EIAT than neurotypical controls. In addition, neurotypical children with elevated levels of autistic traits had poorer interoceptive accuracy than neurotypical children with lower levels of autistic traits. Contrary to the researchers’ expectations, children with ASD and comorbid ADHD did not have lower

interoceptive accuracy than children with ASD alone.

The researchers conclude, “Difficulties in sensing and comprehending internal bodily signals in childhood may be related to both ASD and ADHD symptoms.” However, they note that their sample size was small and that their focus was limited to cardiac interoception, which is only one aspect of interoception.

“Decreased interoceptive accuracy in children with autism spectrum disorder and with comorbid attention-deficit/hyperactivity disorder,” Han-xue Yang, Han-yu Zhou, Ying Li, Yong-hua Cui, Yang Xiang, Rong-man Yuan, Simon S. Y. Lui, and Raymond C. K. Chan, *Autism Research*, January 27, 2022 (online). Address: Raymond C. K. Chan, Institute of Psychology, Chinese Academy of Sciences, 16 Lincui Road, Beijing 100101, China, rckchan@psych.ac.cn.

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/finding-a-clinician>

Quotable....

“[A]utism theories, assessments and interventions have tended to gloss over the extent to which motor skill differences affect autistic people. A burgeoning literature, however, suggests that broad motor differences are more relevant than has historically been appreciated for understanding, assessing and supporting people on the spectrum.

“Three large-scale prevalence studies have... confirmed that general motor differences are pervasive, clinically significant and underrecognized in autism. Up to 87 percent of autistic children exhibit motor challenges, yet only a small number receive a motor-specific diagnosis (15 percent) or treatment (32 percent), revealing a considerable clinical gap. Based on these findings, motor challenges are at least as prevalent in people with autism as either cognitive or language impairment, which are both DSM specifiers and widely thought to shape individual presentations, treatment recommendations and outcomes....

“Treating fundamental motor difficulties might help with problems misinterpreted as oppositional behavior. For example, a child with autism may actively resist getting ready for school because delayed fine motor skills make daily tasks such as tying shoes or buttoning a coat particularly challenging. Directly supporting motor skill differences may provide a novel path for improving functional outcomes, and reducing frustration, across a variety of daily-living domains.”

—Ashley de Marchena and Casey Zampella, “Motor skills in autism: a missed opportunity,” *Spectrum News*, January 4, 2022

Participants needed for ASD microbiome study

Researchers at Massachusetts General Hospital, Harvard Medical School, and the Autism Research Institute are investigating whether the reason why boys are more affected than girls is related to differences in intestinal bacteria.

We are seeking families to participate in this study who have boy and girl siblings with autism. These families will be mailed stool kits with instructions and will be asked to collect samples. A brief medical history will be taken.

For additional information and enrollment details, please contact Harland Winter, MD by phone, 617-724-2004, or by email at GenderDimorphism@autism.org.

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- Networking researchers, physicians, and parents to speed the development and dissemination of safe and effective treatment methods.
- Hosting webinars and one of the largest international websites on autism in the world.
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