

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.com

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

Large-scale study in Britain provides strong support for “extreme male brain” theory of autism

A new study involving more than half a million people offers strong support for the “extreme male brain” theory of autism.

The study, by David Greenberg and colleagues including Simon Baron-Cohen, explored two theories originated by Baron-Cohen:

- The empathizing-systemizing theory predicts that men will score higher on tests of *systemizing*—that is, the drive to analyze and to build rule-based systems—while women will score higher on tests of *empathizing*, or the ability to recognize other people’s thoughts and feelings and the drive to respond to them with an appropriate emotion.
- The extreme male brain theory predicts that on average, people with autism will show a masculine shift compared to the general population, scoring equally high or higher on systemizing and lower on empathizing.

In conjunction with the British television production company Channel 4, the researchers tested more than half a million people including more than 36,000 people with autism. Using brief measures of empathy, systemizing, and autistic traits, they confirmed that in the general population, women typically scored higher than men on empathizing, and

Individuals with autism typically had a shift toward an even higher d-score than males in the general population. The researchers note that d-scores accounted for 19 times the variance in autistic traits compared to other demographic variables, including sex.

men typically scored higher on both systemizing and autistic traits. Individuals with autism had “masculinized” scores, scoring higher on systemizing and lower on empathizing compared to the typical population. The researchers validated their findings in a second sample of more than 14,000 people.

The researchers also calculated the difference between each individual’s score on

the systemizing and empathizing tests (the “d-score”). A high d-score indicates that a person’s systemizing is higher than his or her empathy, while a low d-score indicates the opposite. In the general population, men typically had a shift toward a high d-score, while women typically had a shift toward a low d-score. Individuals with autism typically had a shift toward an even higher d-score

than males in the general population. The researchers note that d-scores accounted for 19 times the variance in autistic traits compared to other demographic variables, including sex.

The researchers say both males and females with ASD exhibited a masculinized shift. “This has relevance for understanding

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Brief screening tool quickly identifies possible GI issues

Gastrointestinal (GI) problems are common in individuals with autism spectrum disorders (ASD), many of whom are unable to communicate their discomfort. Now researchers have developed a screening tool that may allow doctors to quickly and easily identify the children with ASD who are most likely to have GI problems.

Kara Gross Margolis and colleagues began with a long questionnaire developed by the Autism Treatment Network. Noting that medical professionals need to assess patients in a limited amount of time, they carried out a two-stage study designed to identify the most useful questions for doctors to ask. In the first stage of the study, the researchers asked parents of 131 children with ASD to complete the long questionnaire. In the second stage, gastroenterologists unaware of the parents’ responses evaluated each child for the presence or absence of three GI disorders: gastroesophageal reflux disease (GERD), functional constipation, or functional diarrhea. (The researchers note that the term *functional* was used simply to indicate that no organic cause for the problem could be identified.)

Using data from both stages of the study, the researchers identified 17 items that were especially effective in spotting children with the three GI disorders. They report that “this 17-item screen identified children having one or more of these disorders with a sensitivity of 84%, specificity of 43%, and a positive predictive value of 67%.” Margolis notes that while the specificity of the test is low, this was not unexpected in a population that is largely nonverbal. In addition, she notes, “We know that GI conditions are at least fourfold more common in kids with ASD. If we can say

[the screening tool] was over 80% sensitive in accurately picking that up, we are willing to take a high false positive rate to make sure we don’t miss those kids. The alternative is just referring every single child.”

If larger studies confirm the validity of the short questionnaire, Margolis says, parents and doctors will be able to use it as a “road map” for treating individuals with ASD. Positive screens, she says, should result in a referral to a gastroenterologist.

Margolis says that the high rate of GI problems in individuals with autism may be due in part to the antipsychotic medications many are taking, because these drugs can cause constipation. In addition, she notes, gut-brain miscommunication is often impaired in individuals with ASD.

(See related article on page 5.)

“Development of a brief parent-report screen for common gastrointestinal disorders in autism spectrum disorder,” Kara G. Margolis, Timothy M. Buie, J. Blake Turner, Anna E. Silberman, Judith F. Feldman, Katherine F. Murray, Maureen McSwiggan-Hardin, Joseph Levy, Margaret L. Bauman, Jeremy Veenstra-VanderWeele, Agnes H. Whitaker, and Harland S. Winter, *Journal of Autism and Developmental Disorders*, October 22, 2018 (online). Address: Kara G. Margolis, Department of Pediatrics, Division of Gastroenterology, Columbia University Medical Center, New York Presbyterian Hospital, Morgan Stanley Children’s Hospital, New York, NY, kjg2133@cumc.columbia.edu.

—and—

“In kids with autism, short questionnaire may detect GI disorders,” news release, Columbia University, October 22, 2018.

—and—

“New screen quickly identifies GI disorders in kids with autism,” Pauline Anderson, *medscape.com*, November 1, 2018.

Catonia in individuals with ASD may respond very well to manual prompts with gradual fading

Catonic-like symptoms are common in individuals with autism spectrum disorder (ASD), affecting as many as 20% of them. A new case study indicates that prompting can be an effective strategy for overcoming this problem.

Common features of catatonia include increased slowness in speech and movement, passivity, difficulty initiating actions or

completing tasks, reliance on prompts, lack of motivation, and deterioration in functional and social behavior. Symptoms can range from mild to severe. Catatonic symptoms in individuals with ASD are often treated with lorazepam, or, when drug treatment fails, with electroconvulsive therapy.

In the new study by Susan Vener and colleagues, the researchers used positive

reinforcement and manual prompts faded over time to address the symptoms of an 18-year-old girl who had developed symptoms of catatonia at the age of 14. Over time, the girl had stopped talking, following verbal directions, and walking and eating independently. She became immobile, needed significant prompts to engage in daily activities, and maintained rigid postures for extended periods. Medications and nutritional supplements resulted in only minimal improvements.

In the intervention, a therapist initially provided a verbal prompt and full manual guidance during four tasks: blow-drying hair, using a hair barrette, vacuuming, and using a paper shredder. The therapist gradually reduced manual prompts, returning to the previous level if the girl did not successfully perform the activity. Prompts were faded from a firm grasp to a light grasp or touch, and gradually moved from the hand up the arm to the shoulder. Eventually, prompts consisted of shoulder taps, with the therapist using a metronome to gradually decrease the frequency of the taps. Next, the therapist physically moved away from the girl. After that, the researchers changed the setting in which the blow-drying and barrette activities occurred. At each phase, reinforcers and verbal praise were provided only at the completion of the activity.

The researchers say that at the end of the intervention, the girl was able to perform all four tasks independently with a high degree of success, and maintained this ability over a 20-month period. They add that although their paper presented data on the effectiveness of the procedure for only four activities, “the same prompt-fading procedure was used with 15 other activities throughout the course of [the girl’s] school day, and seven activities while in her home environment with her parent and home therapist... [and] the introduction of the prompt-fading sequence resulted in a marked increase in independent responding across activities, locations, clinicians and adults.” They conclude that the girl is “again a functional member of her classroom and her home environment.”

“Increasing behavior incompatible with catatonia in a young adolescent girl with autism spectrum disorder,” Susan M. Vener, Alison M. Wichnick-Gillis, Diamante Badala, and Claire L. Poulson, *Research in Autism Spectrum Disorders*, Vol. 57, January 2019. Address: Susan M. Vener, nyclismv@nycli.org.

—and—
“The nature and prevalence of catatonic symptoms in young people with autism,” Jennifer Breen and Dougal Julian Hare, *Journal of Intellectual Disability Research*, Vol. 61, No. 6, June 2017. Address: Jennifer Breen, Department of Psychology, Royal Holloway University of London, Egham, Surrey, UK.

Study supports extreme male brain theory (cont. from page 1)

the etiology of autism, implicating a biological mechanism involved in neural sexual dimorphism,” they say. “The extreme male brain theory is in line with brain imaging studies which find that autistic females are masculinized in both brain structure and function.” In addition, they say, the theory is consistent with studies showing elevated prenatal sex steroids in ASD as well as elevated circulating sex steroids and elevated rates of polycystic ovary syndrome in females with autism [see related story on page 6].

The researchers emphasize that their findings apply to group averages, not to individuals, and apply only to two gender-related traits—systemizing and empathizing—and not to traits such as aggression. In addition, they note that while individuals with autism often have difficulty recognizing other people’s thoughts and feelings (“cognitive” empathy), they have intact “affective” empathy—that is, the ability to care about others. “Difficulties with cognitive empathy tend to lead autistic people to avoid or be confused by social situations, rather than to act with cruelty,” they say.

Baron-Cohen comments, “This research... pinpoints some of the qualities autistic people bring to neurodiversity. They are, on average, strong systemizers, meaning they have excellent pattern-recognition skills, excellent attention to detail, and an aptitude in understanding how things work. We must support their talents so they achieve their potential—and society benefits too.”

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“Testing the Empathizing-Systemizing theory of sex differences and the Extreme Male Brain theory of autism in half a million people,” David M. Greenberg, Varun Warriar, Carrie Allison, and Simon Baron-Cohen, *Proceedings of the National Academy of Sciences*, November 12, 2018 (free online). Address: David Greenberg, dmg39@cam.ac.uk.

—and—
“Over half a million people take part in largest ever study of psychological sex differences and autistic traits,” news release, University of

The Kids First Initiative: Giving Back to Families

The Hartwell Foundation Kids First initiative seeks to help every family who has a child with an autism spectrum disorder. The goal is to create detailed categories that accurately reflect individual behavior and personality, with the expectation of advancing personalized, targeted approaches for care and intervention that will be more successful than what is available today.

The Kids First approach is conducted using IRB-approved confidential survey methodology by prominent universities. Survey questions are simple, focused on basic behavioral and medical information, and can be completed in about 10 minutes. Results will be shared confidentially with all survey participants. The collected data will provide a unique opportunity for researchers to begin classification of ASD, and as new categories are identified, the effort will expand to more sophisticated requests for information.

We invite you to participate in the Kids First confidential survey, joining a growing network of families, clinicians, and scientists involved in this innovative research project to improve the lives of children and families affected by ASD. To learn more and begin your survey, visit kidsfirst.stanford.edu and when asked, type ARI as your referral code.

—IN MEMORIAM—

ARI’s scientific advisory board recently lost an esteemed member, UCLA researcher Dr. Sydney Finegold, who passed away in July of 2018. Although he “retired” in 2000, Dr. Finegold continued his contributions to medical research with his work on the role of anaerobic bacteria in autism, which he felt had been the most satisfying work for him. Those who worked with him over the years affectionately described him as tireless, with unlimited energy.

EDITORIAL: Stephen M. Edelson, Ph.D.**Autism research: standing on the shoulders of giants**

Isaac Newton once said, “If I have seen further it is by standing on the shoulders of giants.” In the same way, our achievements in the field of autism today stem from the work of early giants in the field—researchers who revolutionized our knowledge about autism and its treatment.

The early days of autism research

Many years passed between the first published paper on autism in 1943 and the start of active research 20 years later. Much of the early research was inspired by Dr. Bernard Rimland’s widely acclaimed 1964 book, *Infantile Autism*, in which he argued convincingly that autism was not a result of emotional neglect—the prevailing theory at the time—but instead had biological roots. In his book and later in a 1968 documentary film, *The Invisible Wall*, Dr. Rimland hypothesized that autism most likely resulted from the interplay of genetics, the environment, and neurology.

Prior to this time, parents often received counseling, while their children were taught play skills. Many researchers and therapists, inspired by Dr. Rimland’s revelations, began readjusting their focus. As a result, physicians and therapists began to treat these children using the same methods they used to treat children with other biologically-based disabilities such as developmental delays.

In these early days, doctors often prescribed strong medications for individuals with autism, such as Haldol, Mellaril, and Tegretol. Therapists frequently used strict behavioral techniques, often referred to as behavior modification, which included physical punishment.

A well-established medical center, UCLA’s Neuropsychiatric Institute, soon took a lead role in studying autism by incorporating both a biological/medical and a behavioral perspective. Because of disagreements on how best to treat challenging behaviors, the principal researcher, Dr. Ivar Lovaas, moved his laboratory to UCLA’s psychology department. About 10 years later, faculty members in the occupational therapy department at USC, including Jean Ayres and Lorna Jean King, began experimenting with various sensory interventions to treat vestibular and tactile sensitivities.

The work of these and other pioneers led to major advances over the next five decades in our understanding about biological, behavioral, and sensory issues in autism. For example:

- Researchers in the biological/medical area uncovered impairments in several systems. These include structural deficits, biochemical imbalances, and abnormal

chemical and electrical activity in the nervous system; immune and metabolic dysfunction; gastrointestinal impairment; and microbiome and nutritional deficiencies.

- New versions of behavioral therapy emerged, with each emphasizing a different approach to fostering cognitive, communication, and social skills and reducing maladaptive behaviors. Some of these include Applied Behavior Analysis (ABA), Pivotal Response Training, Functional Communication, and Floortime.
- Sensory therapy expanded to treat sensory-specific issues, such as deep pressure (e.g., Temple Grandin’s hug machine), hearing (e.g., auditory integration training/Tomatis), tactile (e.g., brushing), vestibular (e.g., controlled swinging), and vision (e.g., ambient prisms and tinted lenses).

The transitional years

During Dr. Rimland’s last year, I moved to San Diego and we began planning the future for the Autism Research Institute. We wanted ARI to maintain its leadership role in the autism research community, and much of our discussion centered on medical/biomedical, sensory, and behavioral issues. Prior to this time, he and I had accumulated much experience, both independently and working together, in all three of these areas.

In addition to bringing attention to genetics, epigenetics, and neurology, Dr. Rimland pioneered the biomedical approach with Drs. Sidney Baker and Jon Pangborn. He also conducted much of the early research on vitamins and minerals, such as vitamin B6 and magnesium. Furthermore, he wrote extensively on healthy nutrition and restricted diets.

Dr. Rimland also helped establish the Autism Society of America, an organization whose mission included informing parents about the benefits of behavioral therapy. In addition, he had much respect for Temple Grandin and learned from her personal experiences dealing with sensory issues. He even wrote the foreword to her first book, *Emergence: Labeled Autistic*, which was later made into a movie on HBO.

For my part, I had been incredibly fortunate to work with many leaders in the autism field. At UCLA, Dr. Lovaas sponsored my undergraduate honors thesis, which was later published. In my thesis, I hypothesized a relationship between biology and behavior. I also learned a great deal about sensory processing from Temple Grandin, who I had

known since our days together in graduate school, and was mentored by several pioneers in sensory processing including Lorna Jean King (vestibular, deep pressure), Guy Berard (hearing), and Melvin Kaplan (vision). During this time, I published some of the early autism research on hearing, vision, and deep pressure.

Starting in the mid-1990s, Dr. Rimland and I worked closely together to raise awareness of the biomedical perspective. Along with volunteers and contractors, we organized annual and semi-annual conferences, published five editions of a book on biomedical treatment approaches, and edited a book of success stories, in which six chapters were written by parents or grandparents who were also medical doctors. In addition, we posted online articles and videos, organized one to two think tanks a year, coordinated an active discussion group for scientists and physicians, and lectured on the biomedical perspective worldwide.

Given our interest in all three major domains—medical/biomedical, sensory, and behavioral—we soon realized that the next step was to encourage and support a multidisciplinary research agenda. In this way, *integrating all three areas could spark a vibrant catalytic synergistic approach to understanding autism*. Such a perspective could energize and expedite research on the underlying causes of autism and the most effective interventions.

Our first joint effort to bring the multidisciplinary perspective to the forefront had actually started 10 years earlier, when we developed the Autism Treatment Evaluation Checklist (ATEC). The ATEC was one of the first, if not *the* first, multidisciplinary assessment tools for autism. This 77-item checklist was designed to evaluate medical/biomedical, sensory, and behavioral issues as well as higher-level systems such as speech/language/communication, sociability, and cognitive awareness.

Many researchers have commented on the ATEC’s usefulness and validity, and it has been employed in numerous research studies. More than 500,000 parents and professionals have completed the ATEC. The checklist is available for no charge online and has been translated into 20 different languages.

ARI today: continuing Dr. Rimland’s legacy

Over the past 12 years, ARI has made great strides in encouraging, integrating, and supporting medical/biomedical, sensory, and behavioral research. We began funding more cutting-edge exploratory research. We also began to offer online webinars for parents

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Research Updates

Siblings of children with ASD may struggle more than other children do

Siblings of children with autism spectrum disorders (ASD) may have more social, psychological, and behavioral problems than other children, a new study suggests.

Carolyn Shivers and colleagues analyzed results from 69 independent studies involving more than 6,600 children with siblings with ASD and more than 21,000 controls. All of the siblings in the studies were at least five years old, and most studies included control groups of neurotypical children or siblings of children with disabilities other than ASD. When studies did not include a control group, Shivers and colleagues compared the siblings of children with ASD with age-matched controls from other studies of comparable size.

Their findings, the researchers say, suggest that siblings of children with ASD have “significantly more negative outcomes” than controls, although the differences were small in magnitude. Specifically, they say, siblings of children with ASD have more internalizing behavior problems such as worrying or withdrawal, more negative beliefs about disability, poorer psychological functioning, poorer social functioning, and poorer sibling relationships. In addition, studies based on clinical evaluations showed that they had more problems with anxiety or depression. However, the researchers detected no significant differences in adjustment, attention problems or hyperactivity, externalizing behavior problems such as aggression or delinquency, coping strategies, or family functioning (although studies based on clinical evaluations hinted at increased problems with ADHD and externalizing behavior problems).

Overall, the researchers say, the siblings of children with ASD functioned at a lower level compared to siblings of children with no disabilities and siblings of children with other intellectual or developmental disabilities.

Shivers notes that whether studies analyzed data collected from siblings or parents, the results were consistent. “To me,” she says, “that says this is a real thing going on: It’s not just siblings being overdramatic or parents being too worried.”

The researchers say their findings indicate that “policymakers and clinicians should make a concerted effort to expand support efforts to include all members of the family [of a child with ASD], including typically developing siblings.”

“Functioning among typically developing siblings of individuals with autism spectrum disorder: a meta-analysis,” C. M. Shivers, J. B. Jackson, and C. M. McGregor, *Clinical Child and Family Psychology Review*, September 3, 2018 (online). Address: Carolyn M. Shivers, Virginia Tech, Human Development and Family Science, 309 Wallace Hall, Blacksburg, VA 24061, shivercm@vt.edu.

—and—

“Siblings of children with autism have social, emotional problems,” Jessica Wright, *Spectrum News*, October 11, 2018.

Social stigma contributes to mental health issues in ASD

Individuals with autism spectrum disorders (ASD) have elevated rates of mental health problems such as depression and anxiety, and a new study indicates that much of this increase is due to social stigma.

In the study, Monique Botha and David Frost collected data from an online survey taken by 111 individuals who identified themselves as autistic. The researchers investigated the relevance of the “minority stress” theory—which posits that members of stigmatized minority groups experience increased stress—to individuals with ASD.

The survey taken by participants delved into six key areas of minority stress, including victimization, “outness” (the degree to which participants disclosed their autism to others), everyday discrimination, expectation of rejection, physical concealment of ASD, and internalized stigma.

The researchers say, “Minority stressors including everyday discrimination, internalized stigma, and concealment significantly predicted poorer mental health, despite controlling for general stress exposure.”

Botha comments, “Traditionally autism and poor mental health were believed to be intrinsically linked, but this is not the case. These findings show that poor mental health of people with autism is instead directly connected with exposure to social stress, which goes beyond the effects of everyday stress that are experienced by others.” She adds that the findings suggest that “taking actions within society to tackle discrimination might significantly reduce rates of poor mental health, and thus suicide in the autistic population.”

“Extending the minority stress model to understand mental health problems experienced by the autistic population,” Monique Botha and David M. Frost, *Society and Mental Health*, October 12, 2018 (online). Address: Monique Botha, University of Surrey, Staghill Campus, Guildford, Surrey GU2 7XH, UK, m.botha@surrey.ac.uk.

—and—

“Social stigma contributes to poor mental health in the autistic community,” Natasha Meredith, *University of Surrey*, October 22, 2018.

Children with ASD have poorer cardiovascular fitness than other kids

Children with autism spectrum disorders (ASD) have reduced cardiovascular fitness compared to neurotypical controls, a new study reports, and the difference does not appear to be due solely to lower physical activity.

In the study, Véronique-Aurélien Bricout and colleagues analyzed data collected from 20 male children with high-functioning ASD and 20 neurotypical controls. Children with cardiovascular problems, respiratory problems, comorbid diagnoses such as epilepsy, or medical treatments that could affect metabolism were excluded.

The researchers used a VO_{2max} test to determine participants’ maximum rate of oxygen uptake during exercise of increasing intensity. This test is used to measure a person’s endurance during prolonged exercise. In addition, they measured the children’s physical activity over a one-week period using accelerometers and performed separate tests to measure flexibility, muscular strength, and explosive power of the legs when jumping.

The researchers report that the children with ASD had lower scores on the VO_{2max} test than controls and had lower effort duration, maximal speed, and treadmill slope. In addition, they exhibited poorer flexibility, muscular strength, and explosive power in the motor skills tests. While children with ASD tend to be less active than neurotypical children in general, the ASD group in this study was as physically active as the controls.

The researchers conclude, “These results suggest that children with ASD are at greater risk for poor aerobic and muscular fitness in adulthood than their unaffected peers, especially as this study involved fit and physically active ASD children. As lower physical fitness is a reliable indicator for poor health outcomes, this study provides an important argument for the systematic implementation of physical activity programs for children with ASD.”

“Reduced cardiorespiratory capacity in children with autism spectrum disorders,” Véronique-Aurélien Bricout, Marion Pace, Léa Dumortier, Flavie Baillieux, Anne Favre-Juvin, and Michel Guinot, *Journal of Clinical Medicine*, October 16, 2018 (free online). Address: Léa Dumortier, ldumortier@chu-grenoble.fr.

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Research Updates

Vasopressin levels in CSF may be biomarker for ASD

Low brain levels of the hormone vasopressin may be a promising biomarker for autism spectrum disorders (ASD), according to new research.

Özge Öztan and colleagues measured oxytocin and vasopressin levels in the cerebrospinal fluid of 36 children with ASD and 36 controls. (Samples were drawn for medical reasons not related to autism.) The researchers found that while the two groups had similar oxytocin levels, the average level of vasopressin in the children with ASD was 66% lower than in the controls. The researchers found that based on vasopressin levels alone, they could correctly identify all but eight children with ASD and nine controls. In addition, they found that in boys but not girls with ASD, lower vasopressin levels correlated with more severe social difficulties.

The researchers say that in addition to being a promising biomarker for ASD, low brain vasopressin levels may be a target for therapy.

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“Cerebrospinal fluid vasopressin and symptom severity in children with autism,” Özge Öztan, Joseph P. Garner, Sonia Partap, Elliott H. Sherr, Antonio Y. Hardan, Cristan Farmer, Audrey Thurm, Susan E. Swedo, and Karen J. Parker, *Annals of Neurology*, October 2018, Vol. 84, No. 4, 611-15. Address: Karen J. Parker, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 1201 Welch Road, Stanford, CA 94305-5485, kjparker@stanford.edu.

—and—
“Low brain hormone levels may be reliable marker of autism,” Nicholette Zeliadt, *Spectrum News*, November 5, 2018.

GI problems may play role in psychiatric issues in ASD

Individuals with autism spectrum disorders (ASD) have elevated rates of both gastrointestinal (GI) symptoms and psychiatric problems such as anxiety and depression, and researchers are reporting new evidence that GI problems may actually contribute to psychiatric symptoms in ASD.

Analyzing data from nearly 2,800 children and adolescents with ASD, Emily Neuhaus and colleagues found that several factors, including a higher number of ASD symptoms, higher verbal IQ, lower adaptive behavior skills, and lower family income, were associated with higher levels of psychiatric symptoms. However, they say, “Levels of GI symptoms accounted for unique variance in psychiatric outcomes over and above these other factors, linking increased GI prob-

lems with increased psychiatric symptoms in children with ASD.”

The researchers say, “With regard to mental health providers, our findings indicate a need to assess for GI symptoms even when those are not the presenting complaint, as they may serve to contribute to the behavioral concerns for which a family is seeking services.” They add that their findings reinforce the need to conceptualize

ASD as a diagnosis affecting multiple neurobiological systems.

(See related article on page 1.)

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“Gastrointestinal and psychiatric symptoms among children and adolescents with autism spectrum disorder,” Emily Neuhaus, Raphael A. Bernier, See Wan Tham, and Sara J. Webb, *Frontiers in Psychiatry*, October 22, 2018 (free online). Address: Emily Neuhaus, eneuhaus@uw.edu.

Local underconnectivity, not overconnectivity, linked to symptoms in ASD

A new study challenges the widely accepted theory that autism spectrum disorders (ASD) involve a combination of long-distance underconnectivity and short-distance overconnectivity in the brain.

Marc-Antoine d’Albis and colleagues note that previous studies investigating short-distance brain connectivity in ASD involved children of differing ages with differing ASD symptoms and used non-specific neuroimaging methods. In contrast, d’Albis and his team recruited a homogenous group of 27 males with ASD but without intellectual disabilities and compared this group to 31 controls using a method specifically designed to study short-distance connectivity.

The researchers report, “In contradiction with the models of short-range overconnectivity in autism spectrum disorder, we found that patients with autism spectrum disorder had a significantly decreased anatomical connectivity in a component comprising 13 short tracts compared to controls. Specific short-tract atypicalities in temporal lobe and insula were significantly associated with clinical manifestations of autism spectrum disorder such as social awareness, language structure, pragmatic skills, and empathy, emphasizing their importance in social dysfunction.”

The researchers say their findings, while preliminary, suggest that repetitive transcranial magnetic stimulation—which appears to affect structural connectivity—may be a useful treatment for the social cognition deficits seen in ASD.

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“Local structural connectivity is associated with social cognition in autism spectrum disorder,” Marc-Antoine d’Albis, Pamela Guevara, Miguel Guevara, Charles Laidi, Jennifer Boisgontier, Samuel Sarrazin, Delphine Duclap, Richard Delorme, Federico Bolognani, Christian Czech, Céline Bouquet, Myriam Ly-Le Moal, Stefan Holiga, Anouck Amestoy, Isabelle Scheid, Alexandru Gaman, Marion Leboyer, Cyril Poupon, Jean-François Mangin, and Josselin Houenou, *Brain*, November 13, 2018 (free online). Address: Josselin Houenou, INSERM U955 “Translational psychiatry” APHP, Hôpitaux Universitaires Mondor 40 rue de Mesly, 94000 Créteil, France, josselin.houenou@inserm.fr.

Free Autism Continuing Education and Webinars

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—January 30, 2019—

TRANSLATIONAL RESEARCH ON BIOMEDICAL INTERVENTIONS FOR AUTISM

Robert L. Hendren, DO

—February 13, 2019—

MOOD AND ASD: NUTRITIONAL STRATEGIES FOR ANXIETY AND DEPRESSION

Vicki Koblner, MS, RDN

—March 6, 2019—

ANXIETY AND ASD

Amy Keefer, PhD, ABPP

—March 13, 2019—

POSITIVE STRATEGIES: CONSIDERING BRAIN AND BEHAVIOR CREATING LEARNING & TREATMENT

Robyn Catagnus, PhD and Bobbie Gallagher, MA

—April 3, 2019—

STRATEGIES FOR SUCCESSFUL DENTAL HYGIENE APPOINTMENTS

Jamie Collins, RDH, CDA

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* We are grateful to our friends at the Johnson Center for Child Health & Development for working in partnership to offer presentations.

New evidence points to significant connection between polycystic ovary syndrome, autism

New findings add to evidence that children of women with polycystic ovary syndrome (PCOS) are at increased risk for autism spectrum disorders (ASD). In addition, the findings indicate that women with ASD are at higher risk for developing PCOS, and that women with PCOS have higher odds of being diagnosed with autism.

PCOS affects five to 15 percent of women of child-bearing age. Women with PCOS over-produce androgens such as testosterone, which influence the development of male characteristics.

In the new research, Adriana Cherskov and colleagues conducted three matched case-control studies using electronic health records from the United Kingdom. The studies investigated:

- The risk of PCOS in women with autism
- The risk of autism in women with PCOS
- The odds of having a first-born child with autism for mothers with or without PCOS

The researchers say their data show that “in the UK, women with autism have an approximately two-fold increase in risk for PCOS, and women with PCOS also had a two-fold increase in rates of autism.” Moreover, they say, “Women with PCOS had 35% increased odds of having a first-born child with autism, after adjusting for comorbid maternal psychiatric diagnosis, metabolic conditions, and complications in childbirth.”

The findings are consistent with previous research by Kyriaki Kosidou and colleagues (see ARRI Vol. 2016, No. 4). Kosidou and coworkers performed a matched case-control study of more than 23,000 individuals with ASD and more than 208,000 controls matched by birth month and year,

sex, and region of birth. In that study, the researchers concluded, “Maternal PCOS increased the odds of ASD in the offspring by 59%, after adjustment for confounders.” Children of mothers with both PCOS and obesity (which also raises androgen levels) had an even greater risk of being diagnosed with an ASD.

Carrie Allison, a coauthor of the new study, comments, “We need to think about the practical steps we can put in place to support women with PCOS as they go through their pregnancies. The likelihood is statistically significant but nevertheless still small, in that most women with PCOS won’t have a child

with autism, but we want to be transparent with this new information.”

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 “Polycystic ovary syndrome and autism: A test of the prenatal sex steroid theory,” Adriana Cherskov, Alexa Pohl, Carrie Allison, Heping Zhang, Rupert A. Payne, and Simon Baron-Cohen, *Translational Psychiatry*, Vol. 8, No. 1, August 1, 2018. Address: Adriana Cherskov, Autism Research Centre, Department of Psychiatry, University of Cambridge, Douglas House, 18B Trumpington Road, Cambridge CB2 8AH, UK, adriana.cherskov@yale.edu.

—and—
 “Women with polycystic ovary syndrome more likely to have a child with autism,” news release, University of Cambridge, October 9, 2018.

Raising a child with ASD can lead to positive personal growth

While much research has focused on the difficulties associated with having a child with an autism spectrum disorder (ASD), a new study from Israel takes the opposite approach: exploring the positive experiences of parents of children with ASD.

In the study, Einat Waizbard-Bartov and colleagues interviewed 19 parents of children with autism. Participants were recruited via Internet messages calling on parents to join a study on growth experiences and positive aspects of parenting a child with ASD.

The researchers report that four “growth themes” emerged from their interviews:

- Many parents described feelings of empowerment and increased personal strength as a result of parenting a child with ASD. The researchers note, “These feelings of empowerment described by parents go beyond the domain of parenting and reflect benefits, gained through parents’ strengthened self-concept, in other life areas.” In addition, they say, nearly all parents mentioned participating in activities that supported other parents of children with ASD. For these parents, the researchers say, feelings of strength manifested themselves in the ability to help others in need.
- A number of parents described growth related to their insights into life or their spiritual or emotional perspectives. In addition, the researchers say, many parents remarked on their growth in their attitude toward parenting a “different” child.
- Many parents commented that their relationships with their spouses became stronger and better, and that they experienced a feeling of “winning a shared victory” as they worked together as parents. Several also commented that their entire family became more united as a result of the experience, while some remarked that parenting a child with ASD made them better parents of their other children as well. In addition, all parents mentioned that parenting a child with ASD led to close ties with friends, professionals, and extended family. Moreover, despite the hardships involved in parenting a child with ASD, the researchers say, “parents in our study spoke of deep and loving connections with their children” and “parents’ intensified involvement with their child with ASD made them view this relationship as special in comparison to relationships with their other children.”
- Many of the parents said that as a result of parenting a child with ASD, they experienced growth in their professional careers. The researchers say, “Parents frequently reported the acquisition of expertise in the field of autism that gradually changed the parent’s professional interest and later enabled a career change.” In addition, many parents became active politically as a result of raising a child with ASD.

The researchers note that their findings do not diminish the hardship of raising a child with autism. “All narratives,” they say, “included references to a crisis period after identifying difficulties in the child’s development or receiving the diagnosis. Descriptions of this period included traumatic images of parents’ worlds as they spoke of hurt, dolefulness, sadness, pain, anxiety, helplessness, and shame.” Rather, they say, their findings show that positive growth can occur for many parents following this crisis phase.

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 “Personal growth experiences of parents to children with autism spectrum disorder,” Einat Waizbard-Bartov, Maya Yehonatan-Schori, and Ofer Golan, *Journal of Autism and Developmental Disorders*, October 26, 2018 (epub prior to print publication). Address: Ofer Golan, Department of Psychology, Bar-Ilan University, 5290002 Ramat-Gan, Israel, ofer.golan@biu.ac.il.

ARRI Survey: Seniors with Autism Spectrum Disorder

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 our online survey at:

https://www.autism.com/adult_survey

We hope the results from this survey will provide insight about the needs and challenges faced by seniors with autism (ages 50 and older) and their support providers, and better inform the autism community, government agencies, and other welfare and health-related organizations about this population’s quality of life issues.

Adding music to therapy sessions may improve social communication, change the brain

Incorporating music into speech therapy for children with autism spectrum disorders (ASD) may enhance social communication and change functional connectivity in the brain, according to a new study.

In the study, Megha Sharda and colleagues randomized 51 young children, 6 to 12 years of age, to 8 to 12 weeks of music-based or non-music intervention. The music-based intervention incorporated musical instruments, songs, and rhythmic cues into activities designed to encourage reciprocal interaction. Children in the control group worked with the same therapist and did similar activities, but without any musical component. Before and after the interventions, researchers assessed the children's social communication skills and performed MRI scans to measure their resting-stage functional connectivity within fronto-temporal brain networks.

The researchers report, "Communication scores were higher in the music group post-intervention." In addition, they say, "Associated post-intervention resting state brain functional connectivity was greater in music vs. non-music groups between auditory and subcortical regions and auditory and fronto-motor regions." In contrast, connections between auditory and visual

regions—an area that is "over-connected" in autism—were lower in the music group compared to the non-music group. Finally, the researchers note, "Post-intervention brain connectivity in the music group was related to communication improvement."

The researchers say their findings are in line with previous research on music and ASD. "Strengths in music processing have been noted since the first description of ASD," they say, "and many studies have reported intact or enhanced musical skills such as absolute pitch, enhanced melodic memory, and contour-processing [identifying patterns of rises and falls] in children with ASD. Greater brain responses to song versus speech in fronto-temporal brain regions and intact emotional responsiveness to music have also been demonstrated. Supporting anecdotal reports from parents and caregivers have described the profound effects music has had on children with ASD."

The researchers conclude, "This study provides the first evidence that 8–12 weeks of individual music intervention can indeed improve social communication and functional brain connectivity, lending support to further investigations of neurobiologically motivated models of music interventions in autism."

"Music improves social communication and auditory-motor connectivity in children with autism," Megha Sharda, Carola Tuerk, Rakhee Chowdhury, Kevin Jamey, Nicholas Foster, Melanie Custo-Blanch, Melissa Tan, Aparna Nadig, and Krista Hyde, *Translational Psychiatry*, October 23, 2018 (free online). Address: Megha Sharda, BRAMS, Department of Psychology, University of Montreal, Pavilion Marie-Victorin, 90 Avenue Vincent D'Indy, Montreal, QC H2V 2S9, Canada, megha.sharda@umontreal.ca.

Autism research: standing on the shoulders of giants

(continued from page 3)

and professionals, which led to producing continuing medical education webcasts specifically developed for physicians.

In addition, we have written numerous articles and editorials, edited books, and lectured on all three areas of research worldwide. We continue to maintain ARI's science newsletter, published quarterly since 1986, and to organize innovative and cutting-edge think tanks that are attracting increasing numbers of researchers.

Not a single puzzle, but many

The image of a puzzle is often used to represent the many components of autism. Our goal is to put more pieces on the table and then to fit them together, either tightly or loosely. What makes this task so challenging is that many of these pieces belong to more than one picture, because autism is a broad term that encompasses multiple subtypes.

We are very hopeful that our current research into subtyping, an effort that builds and expands on decades of work done by giants in the field such as Dr. Rimland, will empower us to determine which pieces belong to which puzzles. As a result, we will be able to identify the most promising treatments and research avenues for each individual subtype—a breakthrough that we believe will once again revolutionize the field of autism.

Noise-attenuating headphones: benefits, barriers reported

A new study suggests that noise-attenuating headphones may help children with autism spectrum disorders (ASD) better tolerate noise at home, at school, and in the community, although there are some barriers to using them.

Participants in the study included 10 parents, 5 teachers, and 15 children who were 6 to 12 years of age and exhibited auditory hypersensitivity. The children wore the headphones for two to four weeks, spending half the time wearing around-the-ear headphones and the other half wearing in-the-ear versions. The researchers interviewed the parents and teachers following the intervention.

Parents and teachers reported a number of benefits of the headphones, primarily in the school setting. These included increased participation and enjoyment in tasks; reductions in disruptive behaviors; decreased anxiety; improved attention and focus; and reductions in escaping (elopement). Parents or teachers commented that the headphones helped children tolerate noise in restaurants, at assemblies, at recess, in the cafeteria, and during noisy activities such as riding the train, attending a wedding, or participating in a fire drill. Several parents and teachers also reported that the headphones empowered children to regulate their own behavior, predicting when they needed the headphones and initiating their use.

However, the study also revealed several downsides of headphone use. Some parents and teachers expressed concern that the children would become overly dependent on the headphones, while others worried about the possible stigma created by the over-the-ear version. Some of the children found the in-ear headphones uncomfortable, and some had more difficulty paying attention or hearing and engaging in conversations due to the sound-blocking nature of the around-the-ear headphones. Other issues raised included the cost of the headphones and the fact that children or caregivers sometimes forgot to bring them along to noisy environments.

While many children initially resisted wearing the headphones, parents and teachers found that preparing the children adequately—for instance, by modeling the use of the headphones, explaining their purpose, and allowing other children in the classroom to use them in order to reduce the stigma—led to acceptance.

"Impact of noise-attenuating headphones on participation in the home, community, and school for children with autism spectrum disorder," Beth Pfeiffer, Shelly Rae Erb, and Laura Slugg, *Physical & Occupational Therapy in Pediatrics*, September 28, 2018, pp. 1-17. Address: Beth Pfeiffer, Department of Rehabilitation Sciences, Temple University, 3307 North Broad Street, Philadelphia, PA 19140, bpfeiffe@temple.edu.

— AUTISM.JOBS —

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—About ARI—

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

ARI'S WORK INCLUDES:

Conducting and sponsoring research on the causes of and best treatments for autism (more than \$200,000 in research grants awarded last year), with a focus on research that can translate rapidly into help for today's autistic children and adults and their families.

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

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

•
 Sponsoring one or two major think tanks a year, involving researchers and experienced clinicians.

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

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