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Multi-pronged nutritional intervention leads to improved IQ, developmental skills in ASD

A long-term, multifaceted nutritional intervention for individuals with autism spectrum disorders (ASD) may lead to significant improvements in IQ, ASD symptoms, and developmental skills, according to a new study.

James Adams and colleagues enrolled 67 children and adults with ASD in a one-year randomized, controlled, single-blind study. Half of the individuals participated in the nutritional intervention, while the other half served as controls. Fifty non-sibling neurotypical children and adults served as a second control group.

Participants in the treatment group followed a multi-stage protocol:

- Initially, participants received vitamin and mineral supplements.
- On day 30, essential fatty acid supplements were added.
- On day 60, Epsom salt baths were added.
- On day 90, carnitine supplements were added.
- On day 180, digestive enzymes were added.
- On day 210, participants also began eating a healthy, gluten-free, casein-free (GFCF) diet.

Of the 37 families involved in the treatment group, 28 completed the study. The researchers report, "There was a significant improvement in nonverbal intellectual ability in the treatment group compared to the non-treatment group based on a blinded clinical assessment." Nonverbal IQ rose by 6.7 points in the treatment group, compared to a slight drop in IQ for the controls with ASD.

Semi-blinded assessments showed that developmental age increased by 18 months in the treated group, compared to four months for the controls with ASD. Symptoms of autism also improved more in the group receiving treatment than in the control group, as did gastrointestinal symptoms.

Adams and colleagues report that three children in particular experienced exceptional results:

—A nine-year-old girl initially had very little strength or energy and was unable to get into the family van, climb stairs, or get off the floor by herself. In addition, she needed to use a wheelchair for outings. Following the intervention, her energy increased, she no longer needed the wheelchair, and she began skipping. In this case, improvement appeared to be due to carnitine supplementation.

—A 27-year-old man suffered from severe urinary retention and needed daily catheterization. Four days after the introduction of the healthy GFCF diet, he was able to urinate on his own. His difficulty in urinating returned any time he ate dairy and disappeared when he went back on the diet.

—A seven-year-old boy had severe pica. Within one week of starting the healthy GFCF diet, his pica disappeared.

The researchers say, "The three case studies suggest that nutritional deficiencies and/or food intolerances can have significant effects, and the comprehensive nutritional/dietary treatment protocol is a safe and effective way to identify and treat some intractable problems."

Levels of homocysteine decreased in the treatment group, resulting in normal levels. Levels of some vitamins, but not all, also improved. Individuals in the treatment group experienced few adverse effects during the intervention.

The researchers say that while other studies have investigated the effects of individual nutritional interventions, this study demonstrates that combining these interventions is feasible and safe. They also note that there was no significant correlation of benefits with age, saying that "children and adults of all ages are likely to benefit from this combination treatment."

Thus, they conclude, "We believe that the treatments used here should be considered for use in clinical practice for most children and adults with ASD."

Editor's note: This study was funded in part by the Autism Research Institute.

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"Comprehensive nutritional and dietary intervention for autism spectrum disorder—a randomized, controlled 12-month trial," James B. Adams, Tapan Audhya, Elizabeth Geis, Eva Gehn, Valeria Fimbres, Elena L. Pollard, Jessica Mitchell, Julie Ingram, Robert Hellmers, Dana Laake, Julie S. Matthews, Kefeng Li, Jane C. Naviaux, Robert K. Naviaux, Rebecca L. Adams, Devon M. Coleman, and David W. Quig, *Nutrients*, Vol. 10, No. 3, March 7, 2018 (open access online). Address: James B. Adams, jim.adams@asu.edu.

Study identifies immune, GI differences in children with ASD

A new study reports that children with autism spectrum disorders (ASD) and gastrointestinal (GI) symptoms have alterations in immune system regulation and gut microbiota.

Destanie Rose and colleagues analyzed blood and stool samples from 103 children between 3 years and 12 years of age to assess the children's immune responses and gut microbiota. The researchers divided the children into four groups: children with ASD who had GI symptoms; children with ASD who did not have GI symptoms; neurotypical children who had GI symptoms; and neurotypical children who did not have GI symptoms. The researchers found that:

—Children with ASD and GI issues had higher levels of inflammatory cytokines, such as IL-5, IL-15, and IL-17, compared to children with ASD who did not have GI symptoms.

—Children with ASD and GI symptoms had lower levels of TGFβ1, a protein that is responsible for regulating the body's immune response. Rose notes that this makes these children more prone to inflammation. Interestingly, this protein was deregulated in children with ASD whether they had GI problems or not; this suggests, Rose and colleagues say, that the children without GI symptoms may have other inflammatory conditions such as allergies or asthma.

—Children with ASD and GI symptoms had higher levels of zonulin, a protein that regulates cell junctions in the GI tract and influences intestinal permeability. A "leaky gut" allowing toxins to escape into the body where they can trigger chronic inflammation has been implicated as a factor in autism.

—Children with ASD and GI symptoms had distinctly different gut microbiomes

continued on page 2

Anti-cancer drug reverses social deficits for an extended period in a mouse model of autism

Researchers at the University at Buffalo in New York report that brief treatment with a very low dose of the anti-cancer drug romidepsin can ameliorate social deficits for an extended period of time in animal models of autism.

Luye Qin and colleagues, including senior author Zhen Yan, found that three days of treatment led to three weeks of improvement in mice deficient in a gene called Shank 3—a time span covering the juvenile to late adolescent period. This is equivalent, they say, to several years in humans.

Earlier, the same research team discovered that the loss of Shank 3 disrupts neuronal communications and causes social deficits by affecting the function of the NMDA (n-methyl-D-aspartate) receptor—a receptor that plays a crucial role in regulating cognition and emotion. In the new study, the researchers found that romidepsin could reverse these deficits by restoring gene expression and function via an epigenetic mechanism. (Epigenetic changes increase or decrease the function of a gene without altering DNA structure.)

Many mutations involved in ASD result from chromatin remodeling factors, which change the structure of chromatin—the genetic material in the cell nucleus that condenses into chromosomes. "The extensive overlap in risk genes for autism and cancer, many of which are chromatin remodeling factors, supports the idea of repurposing epigenetic drugs used in cancer treatment as targeted treatments for autism," Yan says.

The researchers explored the effects of a type of chromatin remodeler called *histone modifiers*. These modify proteins called histones that help to organize genetic material in the nucleus in order to regulate gene expression. In particular, they focused on histone deacetylase (HDAC), a family of histone modifiers that are involved in the remodeling of chromatin structure and the transcriptional regulation of targeted genes.

"In the autism model," Yan says, "HDAC2 is abnormally high, which makes the chromatin in the nucleus very tight, preventing genetic material from accessing the transcriptional machinery it needs to be expressed. Once HDAC2 is upregulated, it diminishes genes that should not be suppressed, and leads to behavioral changes, such as the autism-like social deficits." Romidepsin, a highly potent HDAC inhibitor, reduces the effects of HDAC2.

"The HDAC inhibitor loosens up the densely packed chromatin so that the transcriptional machinery gains access to the promoter area of the genes; thus they can be expressed," Yan says.

The researchers found that romidepsin had widespread effects on gene expression. When they conducted genome-wide screening, they found that it restored the majority of the more than 200 genes that were suppressed in the animal model of autism they used.

Yan concludes, "We have discovered a small molecule compound that shows a profound and prolonged effect on autism-like social deficits without obvious side effects, while many currently used compounds for treating a variety of psychiatric diseases have failed to exhibit the therapeutic efficacy for this core symptom of autism."

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"Social deficits in Shank3-deficient mouse models of autism are rescued by histone deacetylase (HDAC) inhibition," Luye Qin, Kaijie Ma, Zi-Jun Wang, Zihua Hu, Emmanuel Matas, Jing Wei, and Zhen Yan, *Nature Neuroscience*, March 12, 2018 (online). Address: Zhen Yan, zhenyan@buffalo.edu.

—and—

"Autism's social deficits are reversed by an anti-cancer drug," news release, University at Buffalo, March 12, 2018.

CDC report: more U.S. children being diagnosed with ASD

A new report from the Centers for Disease Control and Prevention (CDC) reveals that increasing numbers of children are being diagnosed with autism spectrum disorders (ASD).

The CDC determines the prevalence of ASD in the United States based on data from medical and/or school records of eight-year-olds collected from 11 monitoring sites around the country. Its report is issued every other year.

According to the current report, one in 59 children had been diagnosed with ASD by the age of 8 in 2014. This is a nearly 16% increase over 2012.

Boys are still more likely to be diagnosed with ASD than girls; however, the gender gap has narrowed from 4.5-to-1 to 4-to-1, which the CDC says reflects improved diagnosis of girls. The researchers also found that while children in minority groups continue to be under-diagnosed, increasing numbers of black and Hispanic children with ASD are being identified early, apparently due to better awareness and screening. However, despite increased awareness, only 42% of children with ASD had an evaluation for autism by the age of three, even though 85% showed signs of the condition.

The frequency of autism diagnosis varied from site to site, ranging from a low of 1 in 77 children in Arkansas to a high of 1 in 34 children in New Jersey. This appears to be a result of differences in medical and educational services.

The report concludes, "With prevalence of ASD reaching nearly 3% in some communities and representing an increase of 150% since 2000, ASD is an urgent public health concern that could benefit from enhanced strategies to help identify ASD earlier; to determine possible risk factors; and to address the growing behavioral, educational, residential, and occupational needs of this population."

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"Prevalence of autism spectrum disorder among children aged 8 years—Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2014," Centers for Disease Control and Prevention, *Morbidity and Mortality Weekly Report*, April 27, 2018, Vol. 67, No. 6, pp. 1–23.

—and—

"Autism prevalence jumps 16%, CDC says," Jessica Wright, Spectrum, *Scientific American*, April 27, 2018.

Study identifies immune, GI differences in children with autism spectrum disorders

(continued from page 1)

compared to neurotypical children with GI symptoms. Abnormal gut microbiota are also implicated in autism.

Senior researcher Paul Ashwood comments, "Children with ASD with increased inflammation are often those who exhibit the most severe behaviors. This immune activation is not helping these children. It might not be causing autism—we don't know that yet—but it's certainly making things worse."

Editor's note: We are thrilled to see another multidisciplinary research study. Although few, such studies are very much needed to thoroughly understand the underlying biology of autism.

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"Differential immune responses and microbiota profiles in children with autism spectrum disorders and co-morbid gastrointestinal symptoms," Destanie R. Rose, Houa Yang, Gloria Serena, Craig Sturgeon, Bing Ma, Milo Careaga, Heather K. Hughes, Kathy Angkustsiri, Melissa Rose, Irva Hertz-Picciotto, Judy Van de Water, Robin L. Hansen, Jacques Ravel, Alessio Fasano, and Paul Ashwood, *Brain, Behavior, and Immunity*, March 20, 2018 (online). Address: Paul Ashwood, pashwood@ucdavis.edu.

—and—

"Immune system and gastrointestinal deregulation linked with autism," news release, MIND Institute, April 17, 2018.

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EDITORIAL: Stephen M. Edelson, Ph.D.

ARI's Autism Treatment Evaluation Checklist (ATEC): Its Development and Application

The Autism Treatment Evaluation Checklist, or ATEC, is one of the most widely used assessment tools in the autism community. The checklist is designed to evaluate the efficacy of treatments as well as to monitor how an individual progresses over time. The ATEC is used by parents and researchers as well as by schools, medical and behavioral clinics, and insurance companies. Over a half million ATECs have been completed over the past two decades.

The ATEC contains a total of 77 questions that are classified into four subscales: Speech/Language/Communication, Sociability, Sensory/Cognitive Awareness, and Physical/Health/Behavior. The ATEC is available free of charge online; you can download it at www.AutismTreatmentEvaluationChecklist.com. Besides English, the ATEC is available in 20 different languages, such as Chinese, Czech, Japanese, French, Italian, and Spanish.

History / Background

Dr. Rimland and I developed the ATEC in the mid 1990s. During this time, the Autism Research Institute (ARI) was conducting a series of research studies on the efficacy of various sensory interventions. In addition, we were encouraging the autism research community to evaluate various biomedical and nutritional interventions, and we wanted to recommend a set of valid and reliable assessment tools.

When searching for appropriate assessment measures, I realized that the results of countless studies relied on checklists designed to *diagnose* autism rather than to evaluate *treatment efficacy*. Given that the goal of these studies was to investigate the effectiveness of interventions as objectively as possible, we realized that many if not most of these results could be considered questionable.

Dr. Rimland and I wrote to the authors of many diagnostic checklists and soon confirmed what we had suspected: Those diagnostic checklists were not validated to evaluate changes in medical co-morbidities or behavior. Although our resources were limited, we decided to develop a checklist to properly evaluate changes in individuals with autism.

At that time, we were aware of the Aberrant Behavior Checklist (ABC). Although the checklist was created to assess behaviors in those who were intellectually challenged, some researchers used it to evaluate behaviors in those with autism. Given its original intent, the ABC lacks many questions that would be considered autism-specific, such as "avoids contact with others," "anxious/fearful," and "sleep problems."

Several years after the ATEC was released, the Pervasive Developmental Disorder Inventory (PDD-BI) was published (2003). This checklist was validated to assess treatment efficacy in children with autism between 1 1/2 years and 12 years, 5 months of age. The parent form contains 188 questions, and the teacher form contains 180 questions as compared to the 77 questions in the ATEC. In addition, there is a charge to use the PDD-BI.

Development of the ATEC

When developing the ATEC, I first gathered as many autism-related questions as possible from many different sources. Dr. Rimland had written several autism surveys during the previous 30 years, such as the E-2 and the E-3 (109 and 216 questions, respectively); I also collected questions from numerous autism checklists and questionnaires in the public domain. Overall, I compiled more than 1,000 questions.

Dr. Rimland and I then spent several weeks discussing the questions. We removed redundant ones as well as those that would not typically be used to evaluate changes in behavior (e.g., pregnancy and birth complications, child's eye and hair color). We also reworded almost all of them. We then mailed a rough draft to over a dozen researchers and clinicians and asked them to indicate whether each question was clinically relevant and whether the wording was as clear as possible. Based on this input, we felt confident that the questionnaire had face validity, i.e., the questions assessed what they appeared to be evaluating.

Throughout the development of the ATEC, Dr. Rimland would often stress that the final version should fit on a single page; otherwise, he felt that people would not take the time to complete it. After much effort, I was able to format all 77 questions on one sheet.

We then sent out a preliminary draft of the ATEC to parents and professionals who had contacted ARI in the past, and asked them to complete and return the checklist. In the cover letter, we stressed that we were pilot testing the checklist, and we appreciated their taking the time and effort to respond as accurately as possible. We also asked for feedback regarding the wording of the questions and any other thoughts they wanted to share with us.

A total of 1,358 ATECs were returned to ARI over a six-month period. We then analyzed the data to examine whether the questions within each of the four subscales were assessing the same issue. This was accomplished by calculating a Pearson split-half (internal consistency) coefficient in which the responses to the odd-numbered questions were compared to the even-numbered questions within each subscale and between subscales. For this analysis, one would expect relatively high association between questions within each subscale, and relatively low association between the subscales. For example, questions within the Sociability subscale should be highly correlated with one another, and these questions should have a lower correlation with those in the Sensory/Cognitive Awareness subscale. The results were quite impressive, with correlation coefficients ranging from 0.815 to 0.920.

We then publicized the availability of the ATEC through ARI's e-newsletters, conferences, and websites. Initially, the checklist was available in hardcopy only, and eventually, it was uploaded to ARI's autism.com website.

Published research studies

Over the years, a number of researchers have used the ATEC and have commented on its usefulness. Klaveness et al. (2013) employed the ATEC to investigate the effectiveness of dietary interventions and noted the checklist's high level of reliability. In a study examining the usefulness of iPad intervention, Whitehouse (2017) stated that the scores of the ATEC had "internal consistency and adequate predictive validity." In a five-year study, Magiati et al. (2011) monitored the progress of 22 school children and found that the ATEC had high internal consistency and was comparable to other standardized measures.

More recently, I have been working with Dr. Andrey Vyshedskiy and his colleagues on a series of studies on the usefulness of the ATEC. In a recent study involving 2,649 cases, we were able to develop a "growth" chart for autism which maps out, on average, the trajectory of expected ATEC scores given one's age and current ATEC scores (Mahapatra et al., 2018).

Additional Comments on the ATEC

I have several helpful suggestions for parents or professionals completing the ATEC. One is to consider the individual's behavior during the past three days rather than in a general sense. In this way, the rater does not need to rely too much on memory. An example would be the question on hyperactivity. If the person was hyperactive anytime during the previous three days, then this behavior should be rated as a minor, moderate, or serious problem. However, if there were no signs of hyperactivity during the past three

continued on page 7

Research Updates

Large waist in moms may significantly increase odds of autism in children

Mothers with large pre-pregnancy waist sizes may be significantly more likely to have children with autism compared to mothers with smaller waists, a new study reports.

Previous studies investigating the association between maternal obesity and autism relied on body mass index (BMI). However, Geum Joon Cho, lead author of the new study, says, "BMI is based on weight and does not differentiate between fat mass and lean mass." Waist circumference, in contrast, is an accurate measure of visceral fat, which is body fat within the abdominal cavity. High levels of visceral fat are associated with an increase in inflammatory cytokines, and intrauterine and fetal brain inflammation are believed to play a role in autism.

Cho and colleagues reviewed data on 36,451 mothers who delivered a single live baby between 2007 and 2008 and underwent a National Health Screening Examination within one year of their pregnancy. Their children were followed through 2015, and 265 were diagnosed with autism. The researchers found that children born to mothers with a waist size of 80 centimeters (31.5 inches) or more before pregnancy had a 65 percent increase in the odds of having autism compared to children of mothers with smaller waists.

Cho concludes, "The findings suggest the need for clinicians to monitor for maternal obesity, based on waist circumference, to minimize the risk of development of autism spectrum disorder in offspring." He adds that future studies should focus on whether reducing mothers' waist sizes before pregnancy could lower the risk of their children having autism.

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Cho and colleagues presented their findings at ENDO 2018, the annual meeting of the Endocrine Society in March 2018. Address: Geum Joon Cho, Department of Obstetrics and Gynecology, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea.

Study finds no effect of metformin on memory in individuals with ASD

Increasing numbers of individuals with autism spectrum disorders (ASD) are taking metformin to counteract weight gain caused by antipsychotic drugs such as risperidone (Risperdal). While studies differ as to the results of metformin on memory—with some reporting that it enhances memory, and others reporting that it impairs it—new research suggests that it has neither a positive nor a negative effect on memory in individuals with ASD.

Michael Aman and colleagues enrolled 51 individuals with ASD in their study. Participants were between 6 years and 17 years of age, and all were taking atypical antipsychotic medications, had gained weight, and were enrolled in a trial of metformin for weight management.

Initially, in a 16-week double-blind, randomized trial, half of the group received metformin while the other half received a placebo. In the next open-label phase of the study, all participants took metformin for 16 weeks.

Testing participants' spatial and verbal memory, the researchers report, "No measures differed between participants randomized to metformin versus placebo, at either 16 or 32 weeks, after adjustment for multiple comparisons." They note, however, that more study is needed to support their findings.

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"Effects of metformin on spatial and verbal memory in children with ASD and overweight associated with atypical antipsychotic use," M. G. Aman, J. A. Hollway, J. Veenstra-VanderWeele, B. L. Handen, K. B. Sanders, J. Chan, E. Macklin, L. E. Arnold, T. Wong, C. Newsom, R. Hastie Adams, S. Marler, N. Peleg, and E. A. Anagnostou, *Journal of Child and Adolescent Psychopharmacology*, April 5, 2018 (epub prior to print publication). Address: Michael Aman, michael.aman@osumc.edu.

Infants' pupil responses may help predict later ASD

The pupillary responses of infants to changes in light may help researchers diagnose autism spectrum disorders (ASD) very early in life, according to a new study.

Pär Nyström and colleagues compared the pupil responses of 147 9- to 10-month-old infants at high risk for autism (because they had an older sibling with the condition) to the responses of 40 neurotypical controls. Of the high-risk children, 29 later met criteria for ASD by 36 months of age.

While other studies show that the pupillary responses of older children with autism to changes in light are weaker than usual, the researchers found that they were stronger in infants later diagnosed with ASD than in controls or in high-risk children who did not receive a later ASD diagnosis. Moreover, the amount of pupil restriction in infancy correlated with the severity of later autism symptoms.

The researchers conclude, "This study indicates an important role of sensory atypicalities in the etiology of ASD, and suggests that pupillometry, if further developed and refined, could facilitate risk assessment in infants."

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"Enhanced pupillary light reflex in infancy is associated with autism diagnosis in toddlerhood," Pär Nyström, Teodora Gliga, Elisabeth Nilsson Jobs, Gustaf Gredebäck, Tony Charman, Mark H. Johnson, Sven Bölte, and Terje Falck-Ytter, *Nature Communications*, May 7, 2018 (open access). Address: Terje Falck-Ytter, Uppsala Child & Babylab, Department of Psychology, Uppsala University, SE-75142 Uppsala, Sweden, terje.falck-ytter@psyk.uu.se.

—and—

"New study links strong pupillary light reflex in infancy to later autism diagnosis," news release, Uppsala University, May 7, 2018.

Vasopressin: ASD marker?

A new study involving both monkeys and humans suggests that low levels of vasopressin may be a marker for autism spectrum disorders (ASD).

Karen Parker and colleagues measured levels of oxytocin and vasopressin, two hormones related to social behavior, in the blood plasma and cerebrospinal fluid (CSF) of rhesus monkeys. These animals' social cognition is similar in many ways to those of humans.

Comparing 15 male monkeys with low sociability to 15 male monkeys with high sociability, the researchers found that less-social monkeys had significantly less vasopressin in their CSF than monkeys in the more sociable group. They were able to replicate this finding in a second group of monkeys from a different cohort. Analysis of stored CFS samples from another group of monkeys showed that vasopressin levels remained stable over time.

The researchers also measured vasopressin levels in seven boys with ASD and seven age-matched children without autism, using CSF samples collected via lumbar puncture for unrelated medical reasons. They found that children with ASD had significantly lower vasopressin levels than those without ASD.

Senior study coauthor John Capitanio cautions that while the study points to low CSF vasopressin as a biomarker for the social deficits seen in autism, "we don't know if the deficit is causal.'

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"Arginine vasopressin in cerebrospinal fluid is a marker of sociality in nonhuman primates," K. J. Parker, J. P. Garner, O. Oztan, E. R. Tarara, J. Li, V. Sclafani, L. A. Del Rosso, K. Chun, S. W. Berquist, M. G. Chez, S. Partap, A. Y. Hardan, E. H. Sherr, and J. P. Capitanio, *Science Translational Medicine*, May 2, 2018. Address: Karen Parker, kjparker@stanford.edu.

—and—

"CSF vasopressin a first autism biomarker?," Batya Swift Yasgur, Medscape, May 9, 2018.

Research Updates

Marked differences in the developmental trajectory of the amygdala seen in ASD

A new study indicates that the developmental trajectory of the amygdala, a brain region that plays key roles in anxiety and social interactions, is altered in individuals with autism spectrum disorders (ASD).

Thomas Avino and colleagues studied postmortem brain tissue samples from 52 individuals—24 neurotypical individuals and 28 individuals with ASD—between 2 and 48 years of age. They found that children with ASD had significantly more neurons in the amygdala than neurotypical controls. However, while the number of neurons in the amygdala increased markedly in neurotypical individuals as they aged into adulthood, it decreased in individuals with ASD. Very young children with ASD had approximately 11% more neurons in the amygdala than controls, while adults with ASD had approximately 20% fewer neurons.

Senior study author Cynthia Schumann says, "We don't know if having too many amygdala neurons early in development in ASD is related to the apparent loss later on. It's possible that having too many neurons early on could contribute to anxiety and challenges with social interactions. However, with time, that constant activity could wear on the system and lead to neuron loss."

She notes, "The amygdala is a unique brain structure in that it grows dramatically during adolescence, longer than other brain regions, as we become more socially and emotionally mature. Any deviation from this normal path of development can profoundly influence human behavior."

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"Neuron numbers increase in the human amygdala from birth to adulthood, but not in autism," Thomas A. Avino, Nicole Barger, Martha V. Vargas, Erin L. Carlson, David G. Amaral, Melissa D. Bauman, and Cynthia M. Schumann, *Proceedings of the National Academy of Sciences*, March 20, 2018 (open access). Address: Cynthia Schumann, Department of Psychiatry and Behavioral Sciences, UC Davis MIND Institute, School of Medicine, University of California, Davis, Sacramento, CA 95817, cschumann@ucdavis.edu.

—and—

"Amygdala neurons increase as children become adults—except in autism," news release, UC Davis MIND Institute, March 20, 2018.

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Cats, children with ASD can form valuable relationships

While children with autism spectrum disorders (ASD) frequently benefit from interacting with dogs, a new study indicates that many also can form valuable relationships with cats.

Lynette Hart and colleagues conducted an internet survey of families that included both a child with ASD and at least one cat, tallying the results from 64 respondents. Afterward, they conducted phone interviews with 16 parents of children with severe ASD, 11 children with milder ASD, and 17 neurotypical children.

The researchers say that most parents commented positively about their cats calming, protecting, or guarding the child with ASD. While cats were more affectionate with neurotypical children, the researchers found that "most were at least moderately affectionate toward the ASD child, with almost 20% very affectionate." In addition, they say, "Most children with diagnosed ASD liked to hold the specified cat (or even always wanted to hold, pet, snuggle, and sleep with the cat)—at similar levels as in typically developing children."

The researchers add, "Importantly, the results revealed that cats showed little aggression with ASD children, and certainly no more than with typical children. It seems that cats in families with an ASD child often provided valuable bonding, attention, and calming affection to the child."

They also note, "Although dogs have the capacity to perform useful tasks and are more interactive with people than cats, they require more attention and care, and some parents reportedly find their ASD child is more compatible with a cat, or that a dog simply would not be a feasible companion for their child."

Hart and colleagues do caution that cats vary greatly in affection and aggression, noting that their study found that cats adopted as kittens were more affectionate and less aggressive to children than cats adopted as adults. They conclude, "Persons seeking to acquire a suitable cat for a child in the family could do well to adopt a calm kitten at weaning, assuring that it has frequent gentle interactions with people of all ages, especially ASD children."

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"Affectionate interactions of cats with children having autism spectrum disorder," Lynette A. Hart, Abigail P. Thigpen, Neil H. Willits, Leslie A. Lyons, Irva Hertz-Picciotto, and Benjamin L. Hart, *Frontiers in Veterinary Science*, Vol. 5, March 2018 (open access). Address: Lynette A. Hart, lahart@ucdavis.edu.

Virtual reality training program improves social skills, results in brain changes in adults with ASD

Researchers testing the results of a virtual reality program designed to teach social skills to adults with autism spectrum disorders (ASD) say that their findings challenge the notion that it is too late at this age for interventions to change the brain significantly.

Daniel Yang and colleagues enrolled 17 young adults with high-functioning autism in a behavioral intervention called Virtual Reality-Social Cognition Training (VR-SCT). The individuals participated in the training for five weeks, completing a total of 10 hours of training. During the intervention, they used computer avatars to interact with a clinician in lifelike social scenarios, receiving real-time feedback as they engaged in job interviews, dates, or other age-appropriate social activities. They underwent functional magnetic resonance imaging (fMRI) scans before and after the intervention.

Tests showed improvements in emotion recognition and "theory of mind" (the understanding that other people have thoughts and feelings) following the intervention. The researchers say they identified three significant brain changes that correlated with changes in social behavior:

—The right posterior superior temporal sulcus, a hub for socio-cognitive processing, showed increased activation to social versus nonsocial stimuli in individuals who had greater gains on a theory-of-mind measure.

—The left inferior frontal gyrus, a region for socio-emotional processing, showed a decrease in activation to social versus nonsocial stimuli that correlated with individual gains in emotion recognition. The researchers say, "It has been reported that there is a right- versus left-hemisphere advantageous difference in face recognition and processing emotional stimuli. Although speculative, it is possible that to successfully process emotional stimuli, one needs to shift from left-hemisphere processing to right-hemisphere processing, and decreasing the use of implicated regions on the left hemisphere may contribute to better emotion recognition. Our result is consistent with this possibility."

—The left superior parietal lobule, a region involved in visual attention, showed significantly decreased activation to nonsocial versus social stimuli. The researchers note that heightened attention to non-social contingencies is considered to contribute to the social difficulties of individuals with ASD.

The researchers say, "These findings extend the window of critical time periods where individuals with ASD may be able to benefit from even short term (10 hours) intervention focused on commonly encountered social exchanges during young adulthood.... Such interventions may not only improve social cognition skills at a critical stage when adults with ASD are needing to develop social skills that support independence, but also strengthen the underlying brain networks to support higher social functioning capacity."

They conclude, "There is currently limited intervention research in adults with ASD. This study moves the field one step closer to the goal of providing scientifically based precise intervention for individuals with ASD into adulthood."

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"Neural mechanisms of behavioral change in young adults with high-functioning autism receiving virtual reality social cognition training: a pilot study," Y. J. Daniel Yang, Tandra Allen, Sebiha M. Abdullahi, Kevin A. Pelphrey, Fred R. Volkmar, and Sandra B. Chapman, *Autism Research*, March 18, 2018 (open access). Address: Daniel Yang, Autism and Neurodevelopmental Disorders Institute, The George Washington University and Children's National Health System, 2115 G Street, NW, Washington, DC 20052, danielyang@gwu.edu.

—and—

"Behavior gains possible in adults with autism, study finds," Michelle Diament, *Disability Scoop*, April 10, 2018.

EEG screening may allow doctors to accurately predict autism spectrum disorders in infants

It may be possible to predict an autism spectrum disorder (ASD) diagnosis with high accuracy in infants using electroencephalogram (EEG) data, a new study reports.

William Bosl and colleagues performed EEGs on 99 infants considered at high risk for ASD (because they had an older sibling with an ASD diagnosis) and 89 low-risk controls. The babies underwent EEGs at 3, 6, 9, 12, 18, 24, and 36 months of age. They also were screened using the Autism Diagnostic Observation Schedule (ADOS).

The researchers used computer algorithms to analyze six components of the EEG signal, using measures of signal complexity. The researchers believe that these measures reflect differences in how the brain is wired and how it processes and integrates information.

> Bosl says, "The results were stunning. Our predictive accuracy by 9 months of age was nearly 100%. We were also able to predict ASD severity, as indicated by the ADOS Calibrated Severity Score, with quite high reliability, also by 9 months of age."

Bosl and colleagues report that overall, the algorithms predicted a clinical diagnosis of ASD with high specificity, sensitivity, and positive predictive value, exceeding 95% at some ages. Bosl comments, "The results were stunning. Our predictive accuracy by 9 months of age was nearly 100%. We were also able to predict ASD severity, as indicated by the ADOS Calibrated Severity Score, with quite high reliability, also by 9 months of age."

The researchers say their findings are consistent with the view that autism begins during early brain development but can take different trajectories. "We believe that infants who have an older sibling with autism may carry a genetic liability for developing autism," study coauthor Charles Nelson says. "This increased risk, perhaps interacting with another genetic or environmental factor, leads some infants to develop autism—although clearly not all, since we know that four of five 'infant sibs' do *not* develop autism."

The researchers note that EEGs are non-invasive, low-cost, and relatively easy to use, and could be incorporated into well baby checkups. Nelson comments, "Their reliability in predicting whether a child will develop autism raises the possibility of intervening very early, well before clear behavioral symptoms emerge."

—

"EEG analytics for early detection of autism spectrum disorder: a data-driven approach," William J. Bosl, Helen Tager-Flusberg, and Charles A. Nelson, *Nature Scientific Reports*, May 1, 2018 (open access). Address: William Bosl, william.bosl@childrens.harvard.edu.

—and—

"Diagnosing autism in infants? EEG algorithms make accurate predictions," Nancy Fliesler, Boston Children's Hospital, May 1, 2018.

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.

Once the data from this survey are collected and analyzed, we will contact those who completed the questionnaire and send them a summary report of the findings.

Intervention teaches children with ASD to respond correctly when lost in the community

Elopement, or wandering off without permission, is a significant danger for children with autism spectrum disorders (ASD). Nearly half of young children with ASD have eloped, and the vast majority of deaths of young children with ASD result from accidental drowning after a child has eloped.

To address this problem, Kelly Carlile and colleagues developed an approach combining high-tech and low-tech help-seeking approaches with training that mimicked common community settings. They tested this approach on six male children with ASD, ranging from 3 years to 14 years of age.

The researchers first showed the children videos, most filmed at local stores, showing the proper high-tech and low-tech responses to being lost. They then gave the children opportunities to practice these skills in a classroom designed to look like a local store, using several different store mock-ups. The mock store set-ups in the classroom included banners, bags, and baskets showing the store logos; pictures of store aisles along with actual store items placed in front of the aisle photos; and adults dressed in store uniforms and wearing store name tags.

In the store setting, the adult escorting the child moved out of view so the child could not see him or her. If the child did not respond correctly, the researchers immediately stopped him, showed a video model of the step, and gave him an opportunity to try again. Manual guidance or verbal prompts were used if needed.

The researchers taught the children different strategies depending on whether the children could identify "lost" versus "not lost" when shown videos:

- The low-tech response taught to children who understood the concept of being lost involved identifying being lost (turning the head to look in different directions); scanning for a store employee; walking up to the employee and saying, "Excuse me, I am lost;" handing over an identification card; and remaining close to the employee.

- The low-tech response taught to children who did not understand the concept of being lost involved remaining in a location until an employee approached; responding to the employee's questions by handing the person a communication card stating that the child was lost; and remaining with the employee.

- The high-tech response taught to the children who understood the concept of being lost involved using an iPhone preloaded with Phone and FaceTime. The children learned to recognize that they were lost, turn on the phone, tap the phone icon, tap the name/picture of the person who accompanied them to the store, wait for the person to answer, tell the person, "I'm lost. I'll tell you where I am," use the camera to show where they were, and then remain in that location.

- The high-tech response taught to the children who did not understand the concept of being lost involved answering a Face Time call on the iPhone, listening for directions to show their location, using the phone's camera to show this location, and waiting at that location.

The children were taken to real stores to assess baseline and post-training skills. The researchers report that accurate performance was near or at zero at baseline and increased to 100% after the intervention. In addition, correct responding remained high across maintenance and postintervention sessions. Moreover, two of the three children who initially could not understand the concept of "lost" were able to do this after the intervention.

The researchers point out that their approach worked even with very young children. In addition, they note that teaching a low-tech response gave children a backup strategy in case they did not have a phone or their phone battery was discharged.

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"Teaching help-seeking when lost to individuals with autism spectrum disorder," Kelly A. Carlile, Ruth M. DeBar, Sharon A. Reeve, Kenneth F. Reeve, and Linda S. Meyer, *Journal of Applied Behavior Analysis*, Vol. 51, No. 2, April 2018, pp. 191-206. Address: Ruth M. DeBar, rdebar@caldwell.edu.

Editorial: ARI's Autism Treatment Evaluation Checklist (ATEC)

(continued from page 3)

days, then this behavior would be rated as "Not a problem."

When evaluating the effectiveness of a treatment, I suggest completing the ATEC at least twice prior to administering the treatment. The time interval could be a few days or a week or more apart. Since a person's behavior varies from day to day, two or more baseline assessments will likely provide a much more accurate representation of the individual's overall behavior status.

It is important to mention that the ATEC is not a diagnostic tool, although research in the future may find that the ATEC, or a subset of its questions, can be used to diagnose autism or possibly a subtype of autism.

Occasionally, someone will write to ARI and urge that we translate the ATEC into his or her language. Unfortunately, we do not have the resources to translate the checklist into additional languages. However, we do encourage the autism community worldwide to consider translating the ATEC. If the accuracy of the translation is confirmed by an independent source, we will be more than happy to upload it and make it available on ARI's website.

For nearly 20 years, the ATEC has been a popular and easy-to-use online assessment tool. Monitoring an individual's behavior from time to time can provide assurance that he or she is moving in a forward direction. The scores may also signal if the individual is regressing or may be suffering from a medical and/or behavior issue that may not be obvious to others. And finally, when trying a new intervention, the results can provide a clear and objective indication as to whether the intervention is truly helpful.

—In Memoriam—

Josh Greenfeld, the father of an autistic son and author of three classic books about him—*A Child Called Noah*, *A Place for Noah*, and *A Client Called Noah*—passed away May 11 at the age of 90.

A friend of Dr. Bernard Rimland's, Greenfeld was a powerful advocate for individuals with autism. A screenwriter as well as an author, he received an Oscar nomination for his screenplay for the movie *Harry and Tonto*.

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32/2

—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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