

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

Measurement of aluminum in brain tissues from ASD donors yields surprising results

The first-ever measurement of aluminum levels in the brain tissue of individuals with ASD has revealed that these levels are “some of the highest values for aluminum in human brain tissue yet recorded.”

Matthew Mold and colleagues used two methods to measure the aluminum in postmortem brain samples from individuals with ASD:

- The researchers used a technique called transversely heated graphite furnace atomic absorption spectrometry to measure the aluminum in samples of cortex from 4 males and 1 female with ASD.
- They also used aluminum-selective fluorescence microscopy to identify aluminum deposits in the brain tissues of 3 females and 7 males with ASD.

The researchers report that the aluminum content of brain tissue in the ASD samples was extremely high. While there was significant variability, they say, “the mean aluminum content for each lobe across all 5 individuals [included in the spectrometry analysis] was towards the higher end of all previous (historical) measurements of brain aluminum content, including iatrogenic disorders such as dialysis encephalopathy [a serious condition caused by aluminum overload during dialysis treatment].” All four male donors whose samples were analyzed by spectrometry had higher aluminum levels than the female donor.

The researchers add, “What discriminates these data from other analyses of brain aluminum in other diseases is the age of the ASD donors. Why, for example, would a 15-year-old boy have such a high content of aluminum in [his] brain tissues? There are no comparative data in the scientific literature, the closest being similarly high data for a 42-year-old male with familial Alzheimer’s disease.”

The results of the fluorescence microscopy were also remarkable. “While aluminum was imaged associated with neurons,” the researchers say, “it appeared to be present intracellularly in microglia-like cells and other inflammatory non-neuronal cells in the meninges, vasculature, grey and white mat-

Mold and colleagues say the aluminum levels seen in the samples from individuals with ASD were toward the higher end of “all previous measurements of brain aluminum content.”

ter.” Aluminum deposits were more prevalent in males than in females.

The researchers conclude, “The fact that we found aluminum in every sample of brain tissue, frozen or fixed, does suggest very strongly that individuals with a diagnosis

of ASD have extraordinarily high levels of aluminum in their brain tissue and that this aluminum is pre-eminently associated with non-neuronal cells including microglia and other inflammatory monocytes.”

“Aluminium in brain tissue in autism,” Matthew Mold, Dorcas Umar, Andrew King, and Christopher Exley, *Journal of Trace Elements in Medicine and Biology*, March 2018, pages 76-82 (available free online). Address: Matthew Mold, the Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, ST5 5BG, United Kingdom.

Folate receptor autoantibodies more common in ASD families

A new study adds to evidence that folate receptor autoantibodies are more common in children with autism spectrum disorders (ASD) and their families than in neurotypical controls.

Folate is a nutrient essential for normal development before birth and during infancy. Autoantibodies to folate receptor alpha (FR α) can block folate transport from the mother to an unborn child during pregnancy, as well as blocking folate transport to the brain in infants.

Edward Quadros and colleagues evaluated 82 children with autism, 53 of their unaffected siblings, 65 of their fathers, and 70 of their mothers for the presence of FR α autoantibodies (Ab), comparing them to 52 unrelated controls. They report, “Overall, 76 percent of the affected children, 75 percent of the unaffected siblings, 69 percent of fathers and 59 percent of mothers were positive for either blocking or binding Ab, whereas the prevalence of this Ab in the normal controls was 29 percent.”

The researchers’ findings extend earlier research showing a significant association of FR α antibodies with ASD. Quadros and his colleagues say that these autoantibodies appear to have a familial origin, and that while they do not directly cause ASD—since the unaffected siblings also had a high prevalence of the autoantibodies—they may contribute to developmental problems when combined with other factors.

The researchers note that while folic acid and folate are actively transported by FR α ,

folinic acid—a different form of folate—is transported via a different mechanism. A separate team of researchers headed by Richard Frye earlier reported that folinic acid treatment results in improvements in language and communication in children with ASD and FR α autoantibodies.

“Although, at present, the clinical trials using folinic acid have some limitations, the consistent positive findings of this safe and well-tolerated treatment raise the potential of a treatment that addresses core symptoms of ASD while also targeting pathophysiological abnormalities,” Quadros and colleagues conclude.

In addition, the researchers say that the high prevalence of folate receptor autoantibodies in parents “raises the possibility of supplementing the parents positive for [the autoantibodies] before pregnancy occurs and the mother throughout the pregnancy with folinic acid to prevent folate deficiency in the fetus.”

[See related article on page 2.]

“Folate receptor autoantibodies are prevalent in children diagnosed with autism spectrum disorder, their normal siblings and parents,” Edward V. Quadros, Jeffrey M. Sequeira, W. Ted Brown, Clifford Mevs, Elaine Marchi, Michael Flory, Edmund C. Jenkins, Milen T. Velinov, and Ira L. Cohen, *Autism Research*, February 2, 2018 (epub prior to print publication). Address: Edward V. Quadros, SUNY Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, NY 11203, Edward.Quadros@downstate.edu.

Bilingualism may help children with autism spectrum disorders develop “set-shifting” skills

Parents in households where two languages are spoken are often advised to speak only one language around a child with an autism spectrum disorder (ASD), but new research suggests that being bilingual may benefit these children’s ability to “set-shift” while not impairing their ability to learn language.

Set-shifting is the ability to easily switch back and forth between tasks in response to demands. Children with ASD are known to be impaired in this ability. Research on neurotypical children suggests that children who continually switch between two languages may develop better set-shifting skills.

To investigate the effects of bilingualism on set-shifting in ASD, Ana Maria Gonzalez-Barrero and Aparna S. Nadig enrolled 40 children between 6 and 9 years of age in their study. Half of the children had high-

functioning ASD, and half were neurotypical. In each group, half of the children were bilingual while the other half spoke only one language.

The researchers measured set-shifting skills using a computerized task called the Dimensional Change Card Sort (DCCS) task, which required the children to sort items based on changing criteria. In addition, they asked parents to fill out a report on the children’s executive function skills (which include planning, set-shifting, working memory, and other skills). They also tested the children’s working memory skills, which they hypothesized would not be affected by bilingualism.

Parent reports revealed that the children with ASD were significantly impaired in set-shifting during daily life compared to the neurotypical controls. The test of working memory administered by the researchers did not show any differences between the two groups.

The researchers report, “Results showed an advantage for bilingual relative to monolingual children with ASD on the DCCS task,” although this advantage in set-shifting was not detected in daily life. As expected, working memory was not affected by bilingualism.

The researchers say that in a recent experiment with an overlapping group of children, they detected a bilingual advantage on a verbal fluency task that included requests such as “name all of the animals you can think of.” This task, they note, measured both lexical skills and multiple executive function skills. “Thus,” they say, “it appears this bilingual

advantage in ASD is not limited to the non-verbal domain or to the particular task we employed in this study.”

The researchers conclude, “We demonstrate that, contrary to common belief, bilingualism is not harmful for children with ASD (e.g., with respect to their language abilities)... and in fact, may provide some advantages, such as mitigating prominent set-shifting difficulties.” They add, “If replicated, this finding could provide critical evidence to inform educational decisions taken by the increasing number of families with children with ASD for whom the use of two or more languages is a valued practice.”

The findings of Gonzalez-Barrero and Nadig are consistent with recent findings by Rachel Reetzke and colleagues, who found that Chinese children who spoke two or more languages did not face additional challenges when it came to learning language skills.

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 “Can bilingualism mitigate set-shifting difficulties in children with autism spectrum disorders?” Ana Maria Gonzalez-Barrero and Aparna S. Nadig, *Child Development*, November 7, 2017 (epub prior to print publication). Address: Ana Maria Gonzalez-Barrero, School of Communication Sciences and Disorders, McGill University, 2001 McGill College, 8th floor, H3A 1G1, Montreal, Canada, ana.gonzalez@mail.mcgill.ca.

—see also—

“Communicative development in bilingually exposed Chinese children with autism spectrum disorders,” R. Reetzke, X. Zou, L. Sheng, and N. Katsos, *Journal of Speech, Language, and Hearing Research*, Vol. 58, No. 3, June 2015.

Inconsistent response to sound detected in ASD

A new study by researchers at Northwestern University offers insights into the auditory processing deficits that are a hallmark of autism spectrum disorders (ASD).

Sebastian Otto-Meyer and colleagues hypothesized that these deficits stem from an inability to respond to sound in a consistent manner. To investigate this theory, they measured the frequency-following response, or FFR, of 12 children with high-functioning ASD and 12 neurotypical controls. They explain, “The FFR is the brain’s response to a periodic sound, including complex sounds such as speech, and gives a nuanced picture of auditory processing.”

Their analysis, which used multiple speech stimuli, found that “children with ASD have less stable FFRs to speech sounds relative to their typically developing peers.” They conclude, “This reduced auditory stability could contribute to the language and communication profiles observed in individuals with ASD.”

The researchers cite evidence that the FFR can be positively affected by language and phonological training. “Therefore,” they say, “it is conceivable that the unstable responses to speech in children with ASD could be improved ... given the right type of auditory and language training. Given the beneficial impacts of music and music therapy on ASD and brain plasticity/cognition, music might be a good place to start.”

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 “Children with autism spectrum disorder have unstable neural responses to sound,” Sebastian Otto-Meyer, Jennifer Krizman, Travis White-Schwoch, and Nina Kraus, *Experimental Brain Research*, January 6, 2018 (online). Address: Nina Kraus, Auditory Neuroscience Laboratory, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, nkraus@northwestern.edu.

Large-scale study points to benefits of prenatal folic acid

A new, large-scale study from Israel suggests that maternal supplementation with multivitamins and folic acid can reduce the risk of children developing an autism spectrum disorder (ASD).

Stephen Levine and colleagues analyzed data collected on 45,300 children born between 2003 and 2007 and followed from birth up to 2015, comparing children who developed ASD to those who did not. They also determined which mothers took prescription

nutritional supplements before and/or during pregnancy. They found that children of mothers who took folic acid, multivitamin supplements, or both types of supplements before and/or during pregnancy had a reduced risk of developing ASD.

The authors conclude that “a reduced risk of autism spectrum disorder in children born to women who used the specified vitamin supplements before and during pregnancy has important public health implications,” but they note that their study does not prove a causal relationship between supplementation and ASD risk.

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 “Association of maternal use of folic acid and multivitamin supplements in the periods before and during pregnancy with the risk of autism spectrum disorder in offspring,” Stephen Z. Levine, Arad Kodesh, Alexander Viktorin, Lauren Smith, Rudolf Uher, Abraham Reichenberg, and Sven Sandin, *JAMA Psychiatry*, January 3, 2018 (online). Address: Stephen Levine, Department of Community Mental Health, University of Haifa, Haifa, Israel.

—and—

“Supplements during pregnancy may reduce autism risk,” Tim Newman, *Medical News Today*, January 5, 2018.

TOLL-FREE CALLING CENTER:

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

833-281-7165

If you are a parent struggling to find help, our volunteers can help you locate the information and resources you need.

GUEST EDITORIAL**Perceptual and Cognitive Disability Research**

Steven J. Orfield, Orfield Laboratories, Minneapolis, MN

Editor's note: The Autism Research Institute has been actively involved in sensory-related research for the past 30 years. An important question is: How can we translate our understanding of sensory challenges to improving the quality of life for those on the autism spectrum? For the past decade, Steven J. Orfield, a colleague of mine and founder of Orfield Laboratories, has focused his efforts on designing sensory-optimal residential, school, and work spaces for those with autism as well as other populations.

Professionals who design building structures typically do not take into account the perceptual and/or cognitive challenges experienced by individuals with various disabilities. Sometimes these challenges are referred to as the “invisible disabilities” within the inclusiveness community. Moreover, when designers are asked to consider the users’ perceptual and/or cognitive disabilities, they often rely on intuition rather than on an agreed-upon, science-based approach. Consequently, the need for objective standards is paramount, given the increasing number of residential facilities, therapeutic clinics, and employment settings currently being designed for those with autism and other disabilities.

The Americans with Disabilities Act (ADA) mandates the need for inclusive design for those with disabilities in order to properly access building structures.¹ Yet, much of ADA is non-specific about perceptual and cognitive disabilities. In this article, I urge professional designers to bear in mind various populations who suffer from perceptual and/or cognitive challenges. These challenges include aging, dementia, autism, mental illness, ADHD, PTSD, SPD, blindness, and deafness. Individuals with these challenges often experience numerous problems including sensory hypersensitivity, limited sensory sensitivity, cognitive problems, and anxiety. Such issues affect at least 40% of the general population². Consistent with the intent of the ADA, individuals do not have full access to a building’s structure if they cannot adequately process information in their surroundings, which can lead to challenges in navigation, attention, work ability, comfort level, and much more.

In 2006, Orfield Labs began a 10-year journey researching perceptual and cognitive disabilities from a user perspective, starting with aging³, dementia⁴, and autism. This included thousands of hours of discussions with top academic and research experts associated with each area of sensation (e.g.,

vision, hearing), and each of the specialized disabilities (e.g., aging, autism, mental illness). Eventually, we came to the realization that one should not design for a diagnosis, but rather, *one should design for the best predictable user experience*. We also concluded that approximately half of the general population needs quiet and simplicity, and the results of disability-based design are preferred by those in the “neurotypical” world.

**Building Costs and Design Research:
The Good News**

Designers and organization administrators often share common assumptions about what *accessible buildings* are, such as (1) they are more expensive; (2) they are more suitable for those with disabilities; (3) they require different solutions for different disabilities; (4) they inhibit many design choices; (5) they require specializations on the design team, and (6) they are less likely to have an aesthetic design. All of these assumptions are incorrect, and they underlie the failure to solve many of the design challenges for those with disabilities.

The Architectural Research Consortium has stated that any modest or large-scale building can be built with a similar budget for both individuals with and without disabilities. For example, a well-designed interior is more important than an expensive façade and an elaborate public entry. Furthermore, aesthetics should be more about a comfortable appearance than expensive finishes. A few years ago, the *Facility Management Journal* (FMJ) featured two of our buildings that were based on these premises.⁵

**The Design Research Concept
of Autism**

During our discussions with many individuals active within the autism community, we came across a common perspective: “When you’ve met one person with autism, you’ve met one person with autism.” Of course, this implies that one should not generalize any aspect of autism to the entire autistic community. With regard to designing a facility to support those on the spectrum, this would imply a nearly impossible task. However, after several years of study as well as discussions with numerous experts, we formed an alternative view on autism. That is, the variability among human beings, with and without autism, is roughly the same. In other words, “when you’ve met one person, you’ve met one person.”

The building design of the Fraser Clinic, located in Woodbury, Minnesota, is the first

autism project worldwide that involved quantifiable perceptual performance standards that focused on the sensory sensitivity of children and adults on the spectrum. Prior to working on this project, we spent much time discussing daily challenges, with an emphasis on sensory sensitivity, with two dozen individuals with Asperger’s syndrome. Their personal experiences were very helpful when forming our approach to designing a user-experience building environment.

As a result of our approach to understanding individuals with autism as well as designing structures for them, we focused our efforts on those who are hypersensitive to sensory sensations in their environment. We do acknowledge that there are at least two other “sensory” groups in autism, including those who are hyposensitive and often crave sensory stimulation (i.e., “sensory seeking”), and those who do not have any sensory challenges.

**Fraser Clinic:
The Design Process**

The Fraser Clinic, directed by CEO Diane Cross and her facilities manager, Dale Raasch, began working with Pope Associates, an architecture firm, on designing a building that would become a branding statement for Fraser. They also consulted with A. J. Paron-Wildes, who is a designer, the mother of a young man with autism, and the author of a number of books about design for autism.⁶ Ms. Paron-Wildes helped balance the structural design with personal experiences encountered by individuals on the spectrum. Orfield Labs was in charge of reducing, or eliminating, potential sources of sensory-related stress and tension within the clinic. This involved user measurements of acoustics, day lighting, thermal comfort, and indoor air quality.

Basically, we did not want the clinic building to be perceived as imposing, institutional, or perceptually noisy. The primary goals were to create a general familiarity and comfort within the clinic and to avoid anything that would trigger hypersensitivity. Our first recommendation was to create a building façade that was more reflective of the sensitivity of children on the spectrum, since many of them suffer from anxiety and are fearful of unfamiliar settings. Staff at Fraser agreed with us, and the design of the new façade was low-key and suggested a welcoming and peaceful building environment.

Furthermore, the design for all spaces within the clinic was nominally similar

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Research Updates

Test for protein damage may help diagnose ASD

A new test that identifies damaged proteins may be useful in diagnosing autism spectrum disorders (ASD) early in life, according to researchers in Britain and Italy.

Analyzing blood and urine samples from 38 children with ASD and 31 neurotypical controls, Attia Anwar and colleagues discovered an association between ASD and damage to proteins in blood plasma caused by two processes: oxidation (in which damage is caused by reactive oxygen species), and glycation (in which damage is caused by the linking of sugars with proteins). The most reliable test they developed revealed that children with ASD had higher levels of the oxidation marker dityrosine and advanced glycation endproducts (AGEs).

Senior study author Naila Rabbani comments that the test “is expected to improve the accuracy of ASD diagnosis from 60-70 percent currently achieved by experts in neurological disorders to approximately 90 percent accuracy” and could potentially be offered at hospitals with or without expertise in neurological disorders.

The children in the study were between 5 years and 12 years of age, and the researchers now hope to repeat the study with younger children to see if their test remains accurate.

“Advanced glycation endproducts, dityrosine and arginine transporter dysfunction in autism—a source of biomarkers for clinical diagnosis,” Attia Anwar, Provvidenza Maria Abruzzo, Sabah Pasha, Kashif Rajpoot, Alessandra Bolotta, Alessandro Ghezzi, Marina Marini, Annio Posar, Paola Visconti, Paul J. Thornalley, and Naila Rabbani, *Molecular Autism*, Vol. 9, No. 3, 2018 (available free online). Address: Naila Rabbani, n.rabbani@warwick.ac.uk.

—and—

“Blood and urine tests developed to indicate autism in children,” news release, University of Warwick, February 18, 2018.

Adults with ASD lack typical response to hearing their names

One of the earliest predictors of autism spectrum disorders (ASD) in children is a diminished orienting response to the sound of their own names, and a new study by researchers in Belgium indicates that this phenomenon occurs in adults with ASD as well.

Annabel Nijhof and colleagues collected data on 21 adults with high-functioning ASD and 21 age- and gender-matched neurotypical

controls. The researchers recorded the participants’ electroencephalogram readings in response to hearing their own first names, the first names of familiar people, and the first names of unfamiliar people, interspersing these within a task that involved identifying an unrelated target sound.

The researchers report that a response called late parietal positivity (PP) occurred in neurotypical participants specifically in response to hearing their own names, indicating enhanced attention; this response did not occur in participants with ASD. The researchers note, “This group difference was associated with diminished activation in the right temporoparietal junction (rTPJ) in the adults with ASD.” A “familiarity effect” was seen on a separate measure, the N1 amplitude, in response to familiar names (own and other), and this did not differ between the two groups.

The researchers say, “Our results contribute to recent theories arguing that social cognition problems in ASD may be caused by a specific deficit in self-other distinction, in which the rTPJ seems to play an important role.”

“Atypical neural responding to hearing one’s own name in adults with ASD,” Annabel D. Nijhof, Monica Dhar, Judith Goris, Marcel Brass, and Jan R. Wiersema, *Journal of Abnormal Psychology*, Vol. 127, No. 1, 2018, 129-38. Address: Annabel D. Nijhof, Department of Experimental Clinical & Health Psychology, Ghent University, Henri Dunantlaan 2, B-9000 Ghent, Belgium, annabel.nijhof@ugent.be.

—IN MEMORIAM—

Jaak Panksepp, Ph.D.

Dr. Jaak Panksepp, a pioneering research psychologist, is best known for his work on the neural circuitry of affection and emotions. This line of study also included examining the role of neuropeptides such as oxytocin and vasopressin. Dr. Panksepp’s 1979 landmark paper titled “A Neurochemical Theory of Autism” discussed the importance of endorphins in understanding autism and suggested reducing these hormones by prescribing an opiate antagonist, such as naltrexone. His insights regarding endorphins set the stage for other researchers to later theorize on the role of gluten and casein on autistic behaviors.

Dr. Panksepp attended several ARI think tanks in the late 1990s and published a quarterly autism newsletter. His dedication to science and humanity, along with his generous and kind heart, will be remembered.

Social media use may be beneficial for individuals with ASD

Moderate use of certain types of social media may increase the happiness of individuals with autism spectrum disorders (ASD), a new study suggests.

Deborah Ward and colleagues recruited 26 individuals with ASD through a school district and via online ads, and another 80 through Amazon Mechanical Turk (MTURK). Participants were diagnosed with Asperger syndrome, autism spectrum disorder, or autism.

All participants provided demographic information. They also completed the Social Media Questionnaire, which identified the sites they used most (if any) and the amount of time they spent on each. In addition, they completed the Subjective Happiness Scale (SHS).

Overall, the researchers say, the average SHS score was slightly lower for study participants than for the general population. However, they say, “Adults with ASD who used social media reported greater subjective happiness than adults with ASD who did not use social media.”

The researchers also detected differences between the types of social media used. “Of the 84 percent of the sample who used social media,” they say, “those who used Facebook, the most popular site, were happier than those who did not.” However, this was not true for users of Twitter, the second most popular site. Happiness levels among individuals using Facebook increased up to the highest hours of usage, falling at that point.

The researchers note, “Face-to-face social interactions pose particular difficulties for people with ASD because of the difficulty in understanding nonverbal communication, decoding thoughts and feelings, and responding quickly. Social media may offer a platform for social connections that alleviates these needs in those with ASD, by offering more time to think about responses and use of verbal text and emoticons.”

They conclude that their research “suggests a novel and practical source of well-being enhancement readily available to those with ASD.”

“Social media use and happiness in adults with autism spectrum disorder,” Deborah M. Ward, Karen E. Dill-Shackleford, and Micah O. Mazurek, *Cyberpsychology, Behavior, and Social Networking*, Vol. 21, No. 3, 2018 (free online). Address: Deborah M. Ward, College of Education, California State University Dominguez Hills, Carson, CA 90747, dward@csudh.edu.

Research Updates

Prolonged-release melatonin improves sleep in kids with ASD

Prolonged-release melatonin may be helpful in treating the sleep problems of children with autism spectrum disorders (ASD), a new study indicates.

Paul Gringras and colleagues in Europe and the U.S. enrolled 125 children in their double-blind study, all between 2 and 17 years of age. Of the children, 121 were diagnosed with ASD and 4 with Smith-Magenis syndrome. All had chronic insomnia.

The children's parents first received instruction on behavioral interventions to improve their children's sleep. Children who did not respond to these interventions then received prolonged-release melatonin, in doses beginning at 2 mg per day and increasing to 5 mg if needed, for 13 weeks.

At the end of the study, the researchers report, 68.9% of children taking melatonin were sleeping better, compared to only 39.3% of children taking the placebo. Children taking melatonin slept nearly one hour longer on average than at the beginning of the study, while those on the placebo slept only nine minutes longer. They also fell asleep nearly 40 minutes faster, compared to 12 minutes for the controls. Neither the children's age nor the presence or absence of comorbid attention deficit hyperactivity (ADHD) affected the results.

Adverse effects were mild and included daytime sleepiness and headaches. No participants with epilepsy in the melatonin group had a seizure during the treatment.

The researchers say that in earlier research using immediate-release melatonin, children fell asleep quickly but woke earlier. This did not occur with the timed-release formula.

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“Efficacy and safety of pediatric prolonged-release melatonin for insomnia in children with autism spectrum disorder,” Paul Gringras, Tali Nir, John Breddy, Anat Frydman-Marom, and Robert L. Findling, *Journal of the American Academy of Child & Adolescent Psychiatry*, Vol. 56, No. 11, November 2017, 948-57. Address: Paul Gringras, Children's Sleep Medicine, Evelina London Children's Hospital, Guy's and St. Thomas', Westminster Bridge Road, London, UK, Paul.Gringras@gstt.nhs.uk.

—and—
“Prolonged-release melatonin improves sleep in children with ASD,” Nick Zagorski, *Psychiatric News*, December 14, 2017.

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Aarti Nair, Ph.D.

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Aquatic program shows multiple benefits

A multifaceted aquatic program designed specifically for children with autism spectrum disorders (ASD) may have benefits that extend beyond improving swimming skills, according to a new study from Italy.

Giovanni Caputo and colleagues tested the effects of a program called Multisystem Aquatic Therapy, or CI-MAT, on 13 children with ASD, enrolling an additional 13 children with ASD to serve as controls. Both groups continued to receive their regular therapy, while children in the study group also underwent 96 45-minute sessions of CI-MAT therapy over the course of 10 months.

The CI-MAT therapy involved three stages:

—Emotional adaptation, in which the children were encouraged to cling to instructors after entering the pool. Once this was achieved, the children were encouraged to explore the pool using their instructors as a “safe base.”

—Swimming adaptation, in which participants learned basic swimming skills.

—Social integration, in which the children participated in traditional group swimming activities and games.

The researchers evaluated the children before and after therapy using the Childhood Autism Rating Scale, the Vineland Adaptive Behavior Scales, and an assessment measuring swimming ability. They report that following treatment, the therapy group showed significant improvements relative to controls in functional adaptation, emotional response, adaptation to change, and activity level. In addition, their swimming skills improved.

The researchers conclude, “Multisystem aquatic therapy is useful for ameliorating functional impairments of children with ASD, going well beyond swimming training.”

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Editor's note: This and other types of aquatic therapy may also help reduce the very high rate of drowning deaths among children with ASD.

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“Effectiveness of a multisystem aquatic therapy for children with autism spectrum disorders,” Giovanni Caputo, Giovanni Ippolito, Marina Mazzotta, Luigi Sentenza, Mara Rosaria Muzio, Sara Salzano, and Massimiliano Conson, *Journal of Autism and Developmental Disorders*, January 8, 2018 (online). Address: Massimiliano Conson, Neuropsychology Laboratory, Department of Psychology, University of Catania “Luigi Vanvitelli”, Viale Ellittico 31, 81100 Caserta, Italy, massimiliano.conson@unicampania.it.

Vibrating pagers: fading intensity, not frequency, is most successful approach for slowing rapid eating

Using a vibrating pager to slow overly-rapid eating by individuals with autism spectrum disorders (ASD) may be more successful if the intervention is faded by reducing the intensity of the pager vibration rather than the frequency of the prompt, according to a new study.

In a single-case study, Amber Valentino and colleagues tested the effects of a pager intervention on a 10-year-old boy who ate very rapidly. Once or twice each day at lunchtime, the researchers conducted a brief session (one to eight minutes) in which they presented the boy with a favored food. An experimenter remotely controlled a pager clipped to the boy's waistband, activating it an average of every 20 seconds. The experimenter physically guided the boy to put his hand on the pager and wait until it vibrated before taking a bite, blocking attempts to eat before the vibration occurred. The boy received verbal praise for waiting between vibrations. The experimenter gradually faded the prompting from full physical prompts to partial physical prompts, and then gave no physical prompts at all.

After nine sessions, the boy was able to successfully wait for the pager prompt 100% of the time. At this point, the experimenter clipped the pager to the boy's waistband and it was set to vibrate every 18 seconds with no other prompts or reinforcement provided.

Once this phase was successful, the researchers tested the results of fading the procedure by reducing the pager intensity from the high setting to the low setting and then muffling it with bubble wrap and a towel. They also tested the effects of fading the number of prompts. They report, "Fading by frequency was ineffective in maintaining an appropriate pace of eating while intensity fading was successful."

While vibrating pagers are an increasingly popular intervention due to their relatively non-intrusive nature, the researchers note that successful techniques for fading pager prompts have not yet been established. They comment, "Fading by intensity may prove more effective because features of the antecedent stimulus (i.e., the vibration) can be altered more gradually with intensity and without any abrupt transfer."

"Evaluation of stimulus intensity fading on reduction of rapid eating in a child with autism," Amber L. Valentino, Linda A. LeBlanc, and Paige B. Raetz, *Journal of Applied Behavior Analysis*, Vol. 51, No. 1, January 2018, pages 177-82. Address: Amber Valentino, TBH, 6475 Sierra Lane, Dublin, CA 94568, avalentino@tbh.com.

Perceptual and Cognitive Disability Research

(continued from page 3)

since many, if not most, individuals on the spectrum have an aversion to change in their environment. As a result, the building had, in general, a more monolithic design. That is, wherever the individual is located in the building, he or she will perceive the spaces as relatively the same. We also avoided using patterns or complex color schemes, graphics, non-representational pictures, and wall coverings. In many ways, our approach was to design a peaceful and simple Zen-like environment.

Building Design Standards

Based on research and experience, Orfield Labs established a set of building performance standards for those with autism and special needs. In general, the goal of these building standards is to reduce *perceptual noise*. These standards were formulated based on 10 years of studying perception and cognition, 20 years of collaborating with national RBD groups such as The Open Plan Working Group and the Architectural Research Consortium, and more than 30 years of hosting national design-research conferences.

The performance standards were based on visual design research and involved defining, modeling, and measuring building environments with respect to perceptual preference and comfort. The results from these analyses provide recommendations regarding the amount of brightness and visual distraction while optimizing feature day lighting along with a pleasant view of the surrounding.

More specifically, the building's perceptual performance standards include:

Visual:

Reflectance, pattern, gloss, color, appearance, lighting level

Aural:

Noise levels, HVAC noise, privacy, reverberation (liveness), footfall noise, speech

Thermal:

Drafts, stagnant air, humidity, thermal asymmetry

Olfactory:

Presence of noticeable smells or odors

Postscript

This article is based on research-based design which has been covered in previous articles in *FJM*.⁷

Biography

Steven J. Orfield, founder of Orfield Laboratories, Inc. in Minneapolis, Minnesota,

has been involved with architectural and product consulting for more than four decades. He began his career by taking a human factors approach to architecture, with an emphasis on acoustics and lighting in relation to their impact on users' experience.

Within 10 years, Orfield Laboratories became the first independent multi-sensory building performance consulting lab in the U.S. Orfield has authored or been featured in more than 350 national and international articles, has written two commissioned white papers for ASID, has organized more than 100 international conferences, and is the founder of the Open Plan Working Group, the Sound Quality Working Group, and the Architectural Research Consortium. He can be reached at steve@orfieldlabs.com or at Orfield Labs (612-721-2455).

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Songs, familiar stories may promote better eye contact

Songs and familiar stories may help children with autism to initiate and maintain eye contact with others, a new study suggests.

Grace Thompson and colleagues comment, “Earlier studies indicate that music is alluring to children with autism, with many preferring music over other stimuli. Further, studies examining fMRI data from children with autism suggest that songs more effectively engage the functional systems within the brain that process both speech and song.”

Thus, the researchers hypothesized that young children with autism might engage visually with a person singing a song to a greater degree than with a person reading a story. In addition, they predicted that familiarity with a story would improve children’s visual attention.

The researchers recruited 16 children with autism, ranging from 7 to 10 years of age, for their study. They selected a familiar and preferred song and story for each child, based on parental reports. They also composed an original song and an original story to present to the children.

Each child watched four one-minute videos in which a research assistant either sang the familiar song, read the familiar story, sang the unfamiliar song, or read the unfamiliar

story. The research assistant played bongos during the songs and held a story book during the stories.

Analyzing the children’s number of eye fixations and how long their eyes dwelled on targets, the researchers found that “children were significantly more likely to look at the performer’s face and body and less at the prop [the bongos or story book] during singing than storytelling and when familiar rather than unfamiliar material was presented.”

They conclude, “Caregivers, educators and therapists can powerfully create a more positive social feedback loop that promotes greater social bonds, pleasure in social interaction, and general social orienting by incorporating naturally motivating play activities such as songs (both familiar and novel) and increasing the child’s repertoire of familiar activities (such as story books).”

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“Fostering spontaneous visual attention in children on the autism spectrum: a proof-of-concept study comparing singing and speech,” G. A. Thompson and L. A. Abel, *Autism Research*, January 22, 2018 (epub prior to print publication). Address: Grace Thompson, University of Melbourne, Melbourne Conservatorium of Music, 234 St. Kilda Road, Southbank, VIC 3006, Australia, graceat@unimelb.edu.au.

Differences in oral microbes detected in children with ASD

While many researchers are studying the gut microbes of children with autism spectrum disorders (ASD), a new study from China examined their dental and saliva microbes, finding significant differences between the children with ASD and neurotypical controls.

Yanan Qiao and colleagues sequenced 111 samples from 32 children with ASD and 27 controls. They report, “Lower bacterial diversity was observed in ASD children compared to controls, especially in dental samples.” Moreover, they say, “pathogens such as *Haemophilus* in saliva and *Streptococcus* in [dental] plaques showed significantly higher abundance in ASD patients, whereas commensals [non-harmful microbes] such as *Prevotella*, *Selenomonas*, *Actinomyces*, *Porphyromonas*, and *Fusobacterium* were reduced.” Further analysis, they say, indicated that ASD was not only associated with a decreased richness of commensals, “but also related to reduced mutual effects within these bacteria.”

In particular, the researchers note the depletion of *Prevotella*. “It does not only interact with the immune system,” they say, “but also plays a key role in degrading a broad spectrum of saccharides [sugars]. Interestingly, it was reported that autistic children may have deficiencies in saccharide metabolism and impaired carbohydrate digestion.” They

add, “*Prevotella* species also have essential genes for the biosynthesis of vitamins, which were reported to mitigate ASD symptoms.”

The researchers also found an association between the pathogenic microbes that were elevated in the children with ASD and the severity of the children’s symptoms. In addition, diagnostic models based on key microbes predicted autism with high accuracy, which the researchers speculate may make these models useful in diagnosing ASD.

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“Alterations of oral microbiota distinguish children with autism spectrum disorders from healthy controls,” Yanan Qiao, Mingtao Wu, Yanhuizhi Feng, Zhichong Zhou, Lei Chen, and Fengshan Chen, *Nature Scientific Reports*, January 25, 2018 (online). Address: Fengshan Chen, studentboss2017@163.com.

ARI’s Deaf/HOH & Blind/Visually Impaired Network is a group of parents, affected individuals and professionals with special interest in people with autism and deafness, or autism and blindness. The group is supported by ASA (the Autism Society of America (1-800-3AUTISM)). Membership is free, and you can join by filling out the online registration form at ARI’s website.

IVIG therapy may improve symptoms and reduce inflammation in individuals with ASD, immune issues

Intravenous immunoglobulin (IVIG) infusion may result in improvements in behavior and reductions in neuroinflammation in a subgroup of individuals with autism spectrum disorders (ASD), a new study reports.

IVIG infusions, which contain antibodies taken from donor blood plasma, are currently used to treat a number of disorders involving immune system dysfunction. Because many individuals with ASD show signs of immune dysregulation and inflammation, Isaac Melamed and colleagues decided to test the effects of IVIG on this population.

The researchers administered high-dose IVIG to 14 individuals diagnosed with ASD

—
Melamed and colleagues report that IVIG therapy resulted in “significant improvements in clinical measurements of stereotyped behaviors and repetitive interests” as well as reductions in markers of inflammation.

and exhibiting evidence of immune dysregulation. Participants underwent IVIG therapy for ten 21-day cycles.

The researchers administered multiple behavioral and cognitive tests before and after the therapy, as well as measuring biomarkers of inflammation. They report, “Overall, in this open-label pilot study, we found significant improvements in clinical measurements of stereotyped behaviors and repetitive interests. Additionally, we observed improvement in primary endpoints of all behavioral/cognitive measures.” Moreover, they say, “significant reductions were seen in the markers of neuroinflammation.”

IVIG was well tolerated, and the researchers say that no participants discontinued their treatment or required reductions in the dosage used or the frequency of administration.

The researchers conclude, “While autoimmune or inflammatory etiologies may not contribute to the majority of cases of autism, they may play a role in select cases of autism. In these select cases, these data suggest that the use of IVIG in some patients with ASD warrants further evaluation in larger clinical trials.”

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“A pilot study of high-dose intravenous immunoglobulin 5% for autism: Impact on autism spectrum and markers of neuroinflammation,” Isaac R. Melamed, Melinda Heffron, Alessandro Testori, and Kellie Lipe, *Autism Research*, February 10, 2018 (epub prior to print publication). Address: Isaac R. Melamed, IMMUNOe Research Centers, 6801 South Yosemite Street, Centennial, CO 80112, melamed@immunoe.com.

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