

Intersections

Waisman Center, University of Wisconsin-Madison

2025
IMPACT
REPORT

Stem Cell Image

Image from the lab of **André Sousa, PhD**, Waisman investigator and assistant professor of neuroscience. Expression of three genes linked to neuronal maturation in the macaque cortex from a study that identified key genes and regulatory networks that guide the maturation of neurons in the primate prefrontal cortex, a brain region vital for complex thinking and linked to neuropsychiatric disorders. They found that the autism-associated gene CHD8 disrupts neuronal development by downregulating RAPGEF4, and that restoring RAPGEF4 expression can rescue normal maturation.

Highlights Include:

Gait as a predictor of Alzheimer's

Waisman-born clinical trials

Finding connection with autism

AI informing research discoveries

Intersections

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Dear Waisman Community,

For more than five decades, the Waisman Center has inspired hope through foundational research discoveries and transformed lives through high quality clinical care and impactful community service. Our strength lies in the breadth and depth of our work, which spans research, service, training, and outreach, all aimed at improving the lives of individuals and families impacted by intellectual and developmental disabilities (IDD) and neurodegenerative diseases.

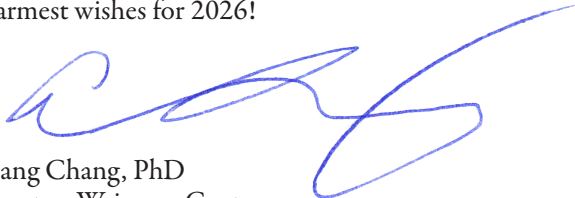
As we look to the future, the promise of new treatments and interventions continues to grow. This year's impact report showcases exciting progress: Waisman-developed innovations entering clinical trials for conditions such as Alexander disease, Down syndrome, and macular degeneration; research linking gait differences to early indicators of Alzheimer's disease in individuals with Down syndrome; our autism treatment program helping young adults build connection and community; advances in artificial intelligence expanding our understanding of cell development; and the vital role of resource guides in helping families navigate life after an IDD diagnosis.

These achievements reflect our unwavering commitment to improving lives—but they also underscore the growing need for support. As traditional funding sources become increasingly uncertain, philanthropic contributions are more critical than ever. Your generosity fuels the innovation and care that define the Waisman Center. It sustains our mission and empowers us to push boundaries, deliver life-changing services, and train the next generation of scientists and clinicians.

You have been an essential part of our journey. With your renewed support, we can build on the foundation we've created together and rise to meet the evolving needs of our community.

On behalf of the entire Waisman Center, thank you for standing with us.

Warmest wishes for 2026!



Qiang Chang, PhD
Director, Waisman Center
Professor of Medical Genetics and Neurology



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Advancing knowledge of human development, developmental disabilities, and neurodegenerative diseases.



Steps toward early diagnosis: Gait changes may predict Alzheimer's in Down syndrome

by Emily Leclerc

Changes in a person's gait, a broad term that refers generally to how a person walks and moves about, may be an early indicator of Alzheimer's disease in individuals with Down syndrome, a new longitudinal study shows. These results, published in the journal *Alzheimer's and Dementia*, by the lab of Waisman investigator Sigan Hartley, PhD, UW-Madison professor of human development and family studies and 100 Women Distinguished Chair in Human Ecology, open the possibility of using gait as an inexpensive and time-efficient screening tool for the development of Alzheimer's disease in Down syndrome.

Down syndrome, also called Trisomy 21, is a genetic condition resulting from a third and extra copy of the 21st chromosome.

Typically, individuals with Down syndrome experience intellectual disability, developmental delays, and are at-risk for various medical conditions including Alzheimer's disease (AD). Individuals with Down syndrome have a 90% lifetime risk of developing AD, which is thought to be primarily driven by the triplicated 21st chromosome. Given this high risk, there has been an uptick in research on how to screen for early symptoms of the disease in people with Down syndrome.

"Over the past 20 or so years, research has found an association between changes in gait – things like shuffling when walking – and Alzheimer's disease in the general population," says Ashlyn Barry, graduate student in Hartley's lab and first author on the paper. "We were really interested to see if gait impairments

“This information can help us say, hey, if you start seeing change in how someone walks – more shuffling, uneven stride lengths, swaying - it might be time to get screened for AD.”

-Ashlyn Barry, graduate student

were also part of Alzheimer’s disease symptoms in people with Down syndrome.” In the general population, gait often begins to deteriorate early on in Alzheimer’s disease and then worsens over time. Hartley and Barry set out to determine if this held true in the Down syndrome community.

Across the span of 32 months, Barry and Hartley measured changes in gait alongside several markers of AD development in 218 adults with Down syndrome. The participants are all part of the Alzheimer Biomarkers Consortium – Down Syndrome (ABC-DS) which is a large multisite research initiative that is funded by the National Institutes of Health (NIH) and focused on finding biomarkers of pathology related to AD in people with Down syndrome with the goal of informing screening practices and interventions. At UW-Madison, ABC-DS is run by Hartley and Waisman investigator Brad Christian, PhD, professor of medical physics and psychiatry.

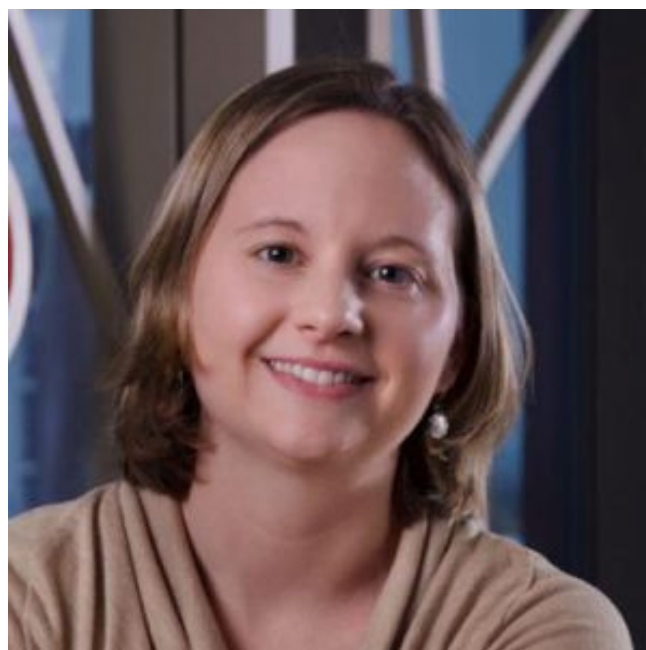
Barry and Hartley found consistent patterns of gait impairment as AD markers changed. Increases in the number of plaques in the brain, changes in brain volume, general cognitive decline, and clinical AD status were all associated with worse gait performance over time. Additionally, they observed that changes in gait could often be seen before the onset of observable changes in AD symptoms.

Establishing changes with gait as part of AD in individuals with Down syndrome can open the door for developing inexpensive and less time-intensive screening tools. “This is very important from a clinical standpoint because typical screening tools for Alzheimer’s disease symptoms generally include lengthy cognitive testing. This is costly and takes a lot of time and requires experts,” Barry says. “However, if instead, we could ask about problems in gait or do quick observations of gait, it has the potential to be a cost-effective and time-effective screening tool.”

Understanding the relationship between gait changes and AD development can also give clinicians and researchers another tool to help empower families with. “This information can help us say, ‘Hey, if you start seeing change in how someone walks – more shuffling, uneven stride lengths, swaying - it might be time to get screened for AD,’” Barry says.

Having visible signs of early dementia can be especially important for individuals with Down syndrome that may have limited verbal skills. “Many of our cognitive tests are not great for individuals with Down syndrome who have limited speech,” Barry says. “So, establishing valid tools of observable functional declines is important for ensuring we can screen for AD in the broad population of individuals with Down syndrome who greatly vary in their cognitive and verbal abilities.”

This study has already opened doors to further questions for Barry and Hartley about gait and AD in Down syndrome. “This paper was our first step in understanding how gait changes in AD,” Barry says. “We now want to delve deeper to better understand these changes. Is it trunk sway or step cadence or something else that changes first?” They are both also interested in understanding the potential for exercise and physical activity to protect against gait changes.



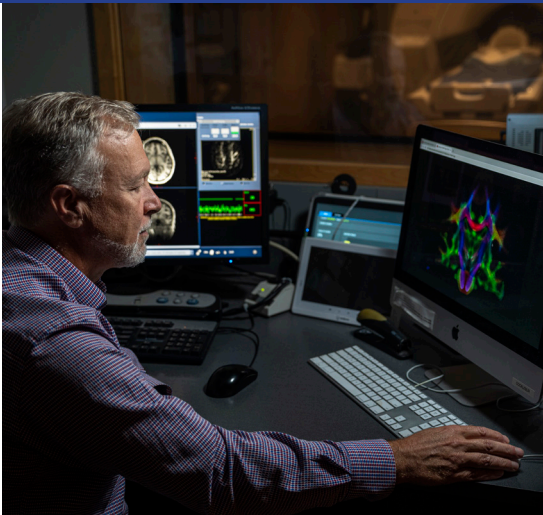
Sigian Hartley, PhD

“We hope that long term,” Barry says, “our work with AD in Down syndrome can lead to better screening tools of AD, inform safety planning, and inform AD prevention efforts for individuals with Down syndrome.” ■

This research was supported by the National Institute on Aging and the National Institute for Child Health and Human Development, Alzheimer’s Disease Research Centers Program, Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Centers Program, National Center for Advancing Translational Sciences, and the National Centralized Repository for Alzheimer Disease and Related Dementias.



Waisman Center Intellectual and Developmental Disabilities Research Center (IDDRC) By the Numbers – FY 2024



Dedicated to finding the causes, consequences, and interventions and treatments for intellectual and developmental disabilities and neurodegenerative diseases.

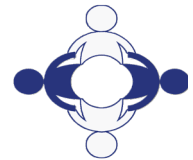
96

federally-funded awards/grants
for a total of

\$87,760,518

in federal funding.

One of only **15** centers of its kind in
the world focused on intellectual and
developmental disabilities.



More than
9,500
children and
families
in the center's
research
registries.



315 employees, **27** postdoctoral
fellows, **57** graduate fellows, and
415 undergraduate and graduate students.

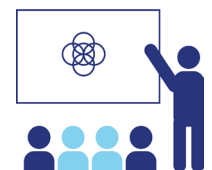
More than **158**
papers published in
academic journals.



Largest multi-disciplinary
center at the University of
Wisconsin-Madison with
45 PIs and
21 affiliates representing
29 different UW
departments and schools.



Hosted **22** Wiley seminars with
more than **1,760** participants.
Held **3** community Day with the
Experts events with more than **550** attendees.





Participants from the Hubbard Lab at the Waisman Whirl Run, Walk & Roll for All Abilities

Friends of the Waisman Center Events

Founded in 1975, **The Friends of the Waisman Center** is a 501(c)(3) organization that supports the center's research, training, service, and outreach missions through fundraising, volunteer efforts, and community outreach. The Friends raise awareness and support for the Waisman Center through three community fundraisers: a spring benefit, a golf outing, and the Waisman Whirl 5K/1M Run, Walk & Roll for All Abilities.

FRIENDS OF THE WAISMAN CENTER SPRING BENEFIT

April 26

Spring benefit donors enjoyed a catered meal by Dave Heide and wine donated by General Beverage and Phillips Wine Company delivered to their home by Friends board members.

FRIENDS OF THE WAISMAN CENTER GOLF BENEFIT

August 5

26 teams of golfers played FORE a good cause at the Friends of the Waisman Center Golf Benefit held at Maple Bluff Country Club. Proceeds from this event help fund a broad range of Waisman activities and programs.

FRIENDS ANNUAL AWARDS & RECEPTION

August 12

The Friends of the Waisman Center present awards each year to Waisman students, staff, and family volunteers. The awards acknowledge outstanding achievements by students, exceptional job performance, skills, and accomplishments of staff, and significant contributions by family volunteers. The awards include a plaque and a \$500 check.

WAISMAN WHIRL RUN, WALK & ROLL FOR ALL ABILITIES

September 27

More than 300 people walked, ran, and rolled to raise awareness and funds in support of the Waisman Center.

BEYOND THE BENCH:

Waisman-born clinical trials

by Charlene N. Rivera-Bonet

Clinical trials serve as the crucial bridge between groundbreaking laboratory research and the eventual approval of new treatments or interventions. At the Waisman Center, researchers like **Albee Messing, VMD, PhD**, and **David Gamm, MD, PhD**, have dedicated decades to transforming innovative ideas into potential therapies, now undergoing rigorous testing to ensure their safety and effectiveness. From tackling rare neurodegenerative diseases to pioneering stem cell applications for vision restoration, their journeys highlight the intricate and lengthy process of bringing scientific discoveries from the lab to the clinic.



Albee Messing, VMD, PhD

The road to clinical trials can take years, often decades, and the journey through the trials themselves is not much shorter. “We had been thinking about clinical trials for a long time. Well in advance of actually having anything. We really started a deliberate search for treatments, maybe 2003 or 2004,” says Messing, professor emeritus of comparative biosciences, whose intervention

for Alexander disease (AxD) is currently in a Phase 1-3 clinical trial. “What is now in clinical trials began coming together as a project in 2013, and by 2016 we had the first real data from the animal work supporting that this idea would potentially work,” he adds.

Messing studies the role of the Glial Fibrillary Acidic Protein (GFAP) in the pathogenesis of AxD, a rare and often fatal neurodegenerative disease. Clinical trials on a new treatment for AxD started in 2021 and are expected to be completed in 2029, with the first set of results expected by the end of 2025. The clinical trial, managed by the company IONIS, is evaluating the safety and efficacy of the drug zilganersen in improving or stabilizing gross motor function in individuals with AxD.

In 2003 David Gamm, professor of ophthalmology and visual sciences, had the idea to use human pluripotent stem cells to help patients with retinitis pigmentosa, age-related macular degeneration, and other diseases of the eye that lead to blindness. “At the time, no one knew how to make retinal cells or tissues from stem cells,” Gamm says. About six years later, in 2009, he changed this and patented the ability to make human retina from stem cells. “And at that point, once we knew we could make early human retina, I said, ‘Okay, this could go somewhere,’” Gamm says. “So that’s when it became a real, achievable goal. A lot needed to be



done, but it was possible.” 15 years later, he received approval from the Food and Drug Administration (FDA) to take this invention into clinical trials.

PHASES OF CLINICAL TRIALS – FDA APPROVAL

Clinical trials are officially divided into four phases (straightforwardly called Phase 1, 2, 3 and 4). However, there are other steps that need to occur before arriving at Phase 1, with the first being discovery and development, such as Messing and Gamm coming up with an idea and doing the research to determine if it works in animal or cell models.

When working in a university research lab, there is a limited number of experiments you can run, or cells you can produce based on funding, space, and human capacity. This becomes more permissive with a company. Before Gamm started the official process for clinical trials, he created a company called Opsis Therapeutics, where he was able to take his product, stem cell-derived retinal cells, and produce it at a higher scale to make it a commercial product for other researchers to use.

“[Making a commercial product] began in 2016 in collaboration with Fujifilm Cellular Dynamics Inc. (FCDI) and by 2021 we had a process that could achieve that goal,” says Gamm. “So, at that point we knew we had a product that could, with some additional

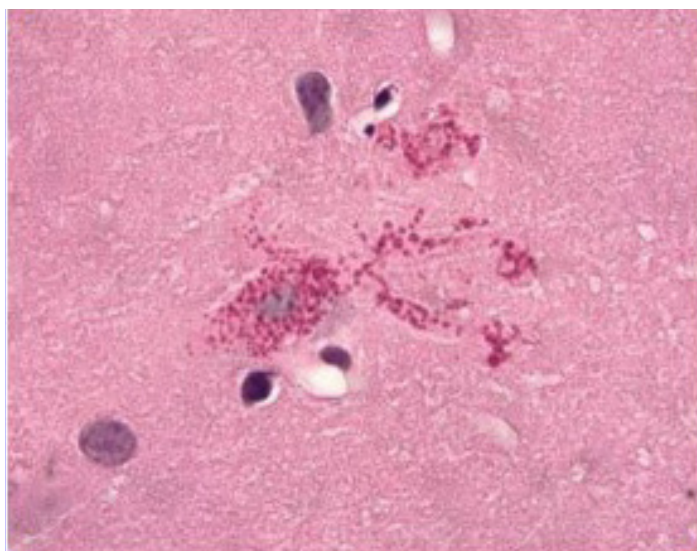
work, get to clinical trial. But we needed a partner to run the clinical trial.”

Opsis Therapeutics and FCDI formed a partnership with BlueRock Therapeutics in 2021, through which Opsis and FCDI would complete the production and testing of the retinal cell products, and BlueRock would run the clinical trials.



The next step was obtaining clearance from the FDA to initiate clinical trials. **Joe Phillips, PhD**, co-founder and preclinical director of Opsis and research scientist in Gamm’s lab led all of the non-clinical work leading up to FDA clearance. “Once we had identified and optimized our first final product, stem cell-derived photoreceptors, then there were a lot of studies that we had to do to develop an investigational new

drug (IND) package for the FDA, which took over two years to complete,” Phillips says. These studies show the FDA that the intervention meets their rigorous safety testing requirements. Once that is approved, they have permission to initiate Phase 1 of the clinical trial. “That was the most eye-opening part.



The hallmark feature of Alexander disease—Rosenthal fibers—is represented by the darker magenta areas in this image of the brain. Image from the Messing lab.

The extensive experimentation, documentation and reporting that's required for an IND package to get clearance from the FDA," Phillips says. "But then the satisfying part is, we successfully did all that and can now move forward with the clinical trial."

PHASES 1 & 2 – A BIG STEP TO START SMALL

Once a clinical trial is handed off to the company who runs it, researchers serve as consultants in the process, but do not participate in the process of recruitment or data collection and analysis to avoid any bias. "Our role was really just doing the animal work, the preclinical studies, providing the rationale and offering some guidance about what they might be looking for in terms of the molecular markers, but all of the clinical work was out of our hands," Messing says. "Once we had done all the mouse and the rat work, we're on the sidelines."

In cases like Gamm and Phillips with Opsi, they participate by developing, manufacturing, and testing the cells that will be used, then serving as clinical and preclinical consultants where their expertise is needed. For the rest, their role is at arm's length to avoid conflict of interests.

This is where **Waisman Biomanufacturing (WB)** steps in for many companies or organizations that utilize their services: manufacturing product during Phases 1 and 2. WB's mission is to accelerate the advancement of novel biotherapeutics and vaccines into clinical trials, which they do by manufacturing biologics such as gene and cell therapies, vaccines, recombinant proteins and plasmid DNA.

WB specializes in the early stages of clinical trials, with a primary focus on Phase 1, and substantial experience in Phase 2. "We are dedicated to enhancing success rates in Phase 1 by developing

products through a 'quality by design' approach, ensuring they possess quality attributes and scalability from the outset," says **Christopher Bartley**, managing director of WB. "It's one area where we've truly excelled. For WB, the quality aspect is the most critical part of any project, and we collaborate closely with our partners to achieve that."

Bartley, along with an outstanding team at WB has contributed to numerous interventions such as HIV vaccines, COVID-19 treatments, a skin substitute product, and therapies for prostate and breast cancer, among many others.

Phase 1 begins with a small number of volunteers, seeking to first test the safety of the intervention. Some interventions may be new, but some may be drugs or treatments that have been already in use but are being repurposed, or evaluated in a different population. The biggest focus of Phase 1 is making sure the treatment is safe. Phase 2 involves a slightly larger group of volunteers and evaluates efficacy – testing if the treatment actually works in addition to its safety.

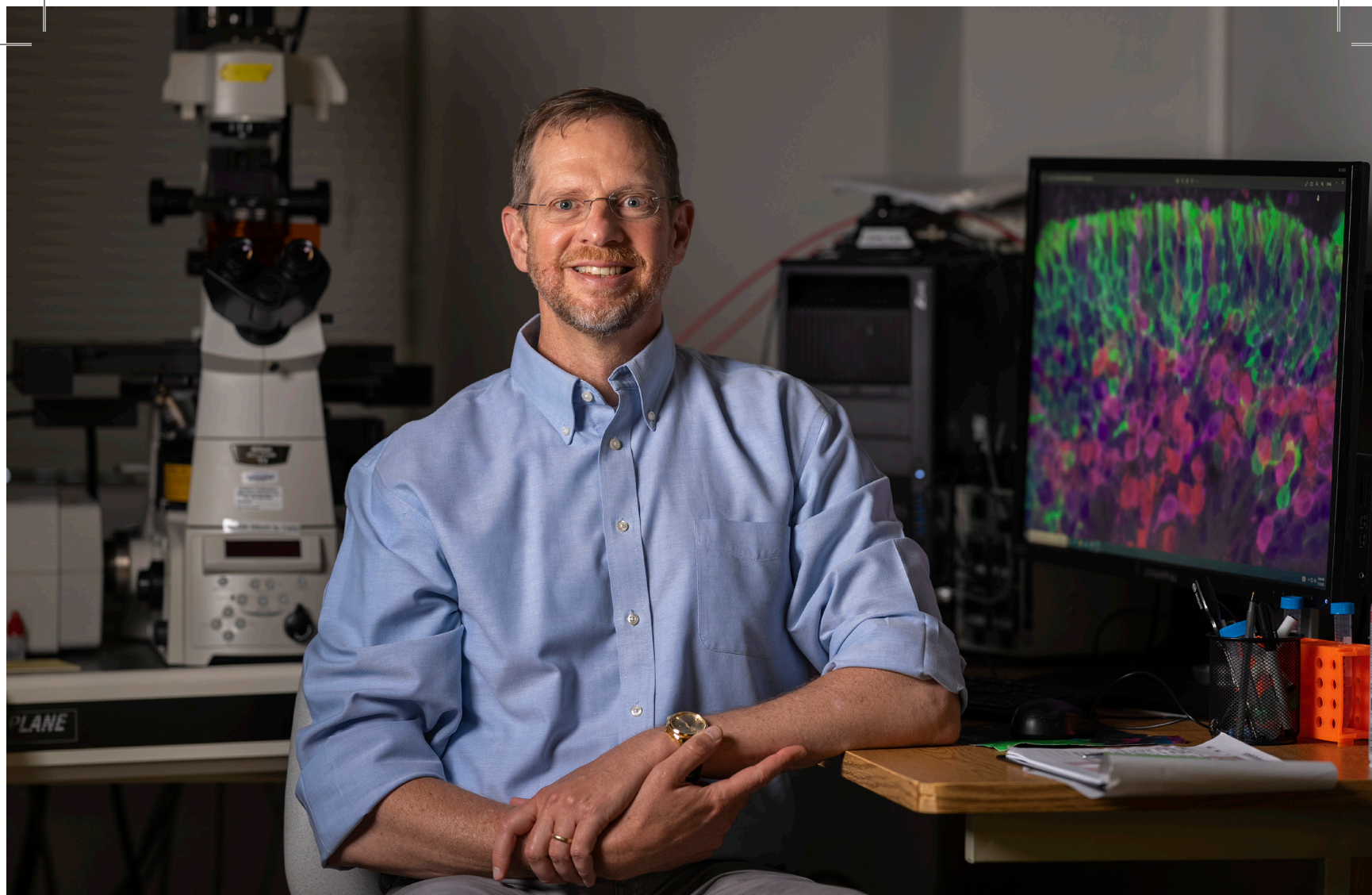


Maria Stanley, MD

Maria Stanley, MD, developmental behavioral pediatrician, is leading two multi-site trials on interventions for children with Down syndrome at Waisman. The first, currently in Phase 2 is for a medication that is already approved for treating ADHD, but its effects on individuals with Down syndrome remain unknown. "Many people who care for people with Down syndrome have observed that responses to medication don't always look the same as they do in other populations. And the thought is that the genetic difference that people with Down syndrome have, could be influencing how they respond to medication," Stanley explains.

Many of the medications that children use have never been studied or approved to be used in children. It is easier, less expensive, and less risky to test it in adults, but "we know kids aren't just little adults. We know that it doesn't always work exactly the same way in kids as adults, and when it comes to special populations with a genetic condition like Down syndrome, we have even less information about that," Stanley says.

"The FDA is primarily concerned with two things during the drug approval process: safety and efficacy," Bartley says. Only about 10% of products that enter clinical trials eventually make it to the market. "The main reasons for failures in the early phases of clinical trials are safety concerns and lack of efficacy," Bartley adds. Financial constraints, such as companies running out of funding - whether it be private investment or limited federal grants - to continue the trials, also contribute to that failure rate.



David Gamm, MD, PhD

photo by Andy Manis

As a product advances through trials, the costs increase related to the size of the trials and the increased stringency for data from the FDA to ensure those standards are met.

PHASE 3 & 4 – GOING SOMEWHERE

An intervention deemed safe and effective goes on to Phase 3, which typically involves a higher number of participants, compares the intervention to existing treatments or a placebo and gathers data on long-term effects.

Stanley's second clinical trial tests a hypoglossal nerve stimulator to treat obstructive sleep apnea. "We see obstructive sleep apnea as a modifiable risk factor for cognitive impairment in people with Down syndrome. So, it's really important to address and treat it," Stanley says.

The hypoglossal nerve stimulator is an implanted device that pushes the tongue forward to help with breathing during sleep. It has been tested and shown to be successful in individuals as young as 13, but the team believes this could benefit an even younger population. "So, we're looking at implanting the device in folks as young as 10, and it is also looking at how specifically can we see the impact on cognition or language through use of the device," Stanley explains. The Clinical Translational Core at the Waisman

Center participates in this trial by providing the cognitive assessments.

Messing's study on an intervention for Alexander's disease is a combined Phases 1, 2 and 3 trial. "It's such a rare disease, with such a small patient population, they figured it would take too long to go through a Phase 1 with healthy controls," Messing explains. It would also put healthy controls at unnecessary risk, "When what they really need to do is find out first of all whether the patient population have somewhat different risks because they start out being sick and have a different molecular profile in their brains," he adds.

Because of how small this patient population is, they extended the trials all over the world, with people participating in Europe, Australia, Japan, Canada, and the United States.

Toward the end of this year 2025, Ionis will release the first set of results that will show whether the intervention is working. "I hope it works. I think the indications are that it's safe," Messing says, because the study would've been stopped otherwise.

What does it look like for the individuals who are participating? Although each trial is different, many of them have similar



One of the clean room facilities in Waisman Biomanufacturing.

structures. For Messing's study, they divide the participants into two groups for a two-year treatment period. For the first year, one group will receive the treatment while the other receives a placebo. The second year, the placebo group joins the treatment group in an open-label phase in which everyone receives the treatment. At the end of the two years, the results can be analyzed.

Both researchers and participants are unaware of which treatment (actual drug or placebo) each group is receiving – called a double blinded study. This helps reduce bias when reporting symptoms and analyzing results.

Phase 4 begins when the treatment has been FDA approved for commercial use, but monitoring of its side effects continues happening after the drug is commercialized.

"We do what we do because we believe in the potential to improve someone's life."
-Chris Bartley, WB managing director

MOTIVATION FOR THE LONG TREK

For Messing, it was the long-standing support of his research from the AxD community that pushed him to work toward clinical trials. "From the beginning, we were in very close contact with the patient community, because we relied on their donations of tissues or DNA to do the work. So, I think very early on, I felt

a responsibility to them, and certainly a scientific interest. If we could figure out what's causing the disease, can we also figure out how to treat it, and alter the course of the disease," he says.

Clinical trials are about finding cures, treatments, and ways to improve people's quality of life.

"We do what we do because we believe in the potential to improve someone's life," Bartley says. "Our ultimate goal is to help those in need, striving to open doors or create avenues for those who aren't getting the treatments they need." ■

PHASES OF CLINICAL TRIALS



Preclinical

Laboratory research and discovery of potential new treatments.



Phase 1

Tests if the treatment is safe and determines proper dose.



Phase 2

Focuses on efficacy of treatment and side effects.



Phase 3

Compares new interventions to existing ones.



Phase 4

Monitors long-term effects after treatment approval.

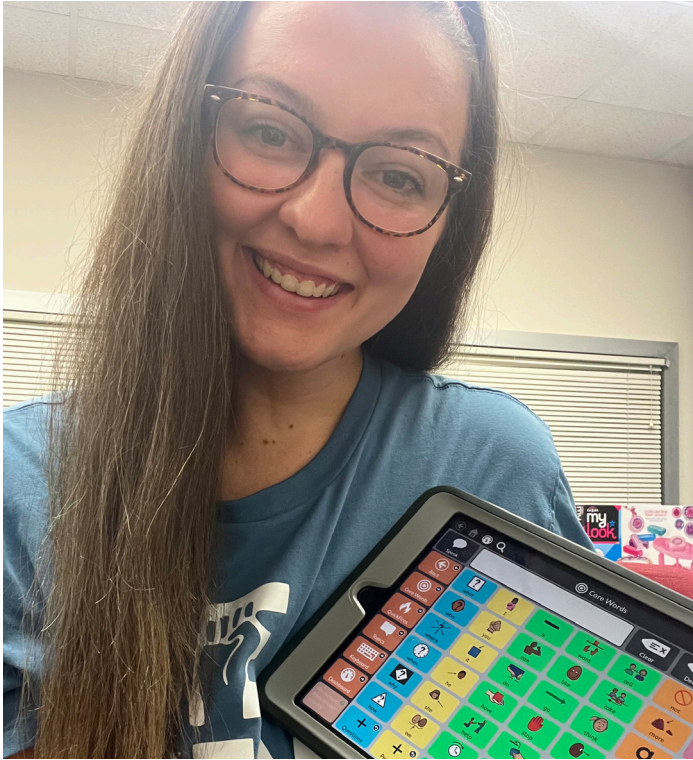
FUNDING SOURCES

Research from the Messing lab that led to clinical trials has been supported by the National Institutes of Health (NIH), Juanma Fund, Rijkaart Fund, United Leukodystrophy Foundation, and Ionis Pharmaceuticals. Gamm's research on technology development has been funded by the NIH's National Eye Institute, Foundation Fighting Blindness, McPherson Eye Research Institute, Retina Research Foundation, Fighting Blindness Canada, U.S. Department of Defense, Trout Family Endowment, and Research to Prevent Blindness. Gamm's preclinical work and the clinical trial has been sponsored by Opsis Therapeutics, Fujifilm Cellular Dynamics Inc. and BlueRock Therapeutics (a subsidiary of Bayer AG). The clinical trials led by Stanley are supported by Duke University and the Massachusetts Eye and Ear Infirmary. ■

LEADING BY EXAMPLE:

Becca Stroschein, MS, CCC-SLP, & Jack Hoselton

The Wisconsin Leadership Education in Neurodevelopmental and Related Disabilities (WI LEND) program trains the next generation of leaders to improve the health and well-being of individuals with disabilities



Becca Stroschein, MS, CCC-SLP

Communication is essential for participating in everyday life. Without it, people can struggle to express their needs, connect with others, and engage with the world around them. For **Becca Stroschein, MS, CCC-SLP**, a speech-language pathologist at the Waisman Center's **Communication Aids and Systems Clinic (CASC)**, helping others find a way to communicate is more than a job—it's a calling.

Stroschein first discovered her passion as an undergraduate volunteer at a nonprofit serving autistic adults. "I realized how powerful it is when someone finds a communication method that works for them," she says. "It opens up their world."

After completing her graduate studies in speech therapy, Stroschein sought a fellowship that would allow her to specialize in augmentative and alternative communication (AAC)—tools and devices that help individuals communicate when speech is limited or unavailable. She found the perfect fit at the Waisman Center, where the CASC fellowship offered a caseload focused entirely on AAC. But there was another key component that drew her in: the **Wisconsin Leadership Education in Neurodevelopmental and Related Disabilities (WI LEND)** program.

WI LEND is a federally-funded training program that prepares professionals, self-advocates, and family members to improve services for individuals with neurodevelopmental disabilities. Integrated into the CASC fellowship, WI LEND gave Stroschein a broader perspective on disability, advocacy, and interdisciplinary care.

"LEND was a huge reason I chose this fellowship," she says. "It helped me become a better speech therapist by showing me the bigger picture—what families go through, what lived experience really means, and how to be a strong voice on a care team."

Now a full-time clinician at CASC, Stroschein reflects on the lessons she's carrying forward. One of the most impactful was learning how to collaborate effectively on interdisciplinary teams—a cornerstone of care at the Waisman Center. During her fellowship, she co-treated patients with occupational therapists and worked closely with other specialists to provide holistic, patient-centered care.

"LEND truly prepares you to be a strong contributor on any interdisciplinary team," she says. "Knowing how to use my voice and advocate for inclusive, accessible services is so important."

Stroschein is also passionate about expanding awareness of AAC. Despite its transformative potential, AAC remains unfamiliar to many professionals and families. She hopes to change that by educating others and building capacity in the field.

"There are people out there who could benefit from AAC but don't even know it exists," she says. "The more we empower teams and families to feel confident using communication devices, the more individuals we can help."

A key part of LEND training involves learning directly from individuals with disabilities and their families. For Stroschein, those experiences were eye-opening. "Going with families to community activities and hearing their stories helped me see life from a whole new perspective," she says. "Their lives are rich and complex, and as clinicians, we need to support every aspect of that."

Stroschein loves her work and feels deeply fulfilled by the impact she's making. "It's magical when someone who hasn't had a way to communicate suddenly finds the right fit," she says. "Helping people express themselves meaningfully is one of the best parts of my job. And I'll carry the lessons from LEND with me for the rest of my career." ■



Jack Hoselton (far left), Stasia Wilson, and Julie Schears meet with local legislators as part of the LEND Disability Advocacy Day.

Jack prefers the use of person-first language with reference to him and his autism diagnosis. The language used in this story reflects that preference.

Jack Hoselton strives to improve society for people with disabilities. His lived experience as a man with autism gives him insight into both the strengths and challenges of the disability community. While a student at Edgewood College's Cutting-Edge Program, he wanted to expand his understanding and advocacy skills so he joined the **Leadership Education in Neurodevelopmental Disabilities (LEND)** Program as a two-year LEND trainee in disability advocacy. Hoselton graduated in May 2025 with a Bachelor of Arts in education studies and began his second year of LEND in fall 2025.

LEND is a federally-funded training program through the Maternal & Child Health Bureau and part of the University Center for Excellence in Developmental Disabilities at the Waisman Center. It prepares emerging leaders—including healthcare professionals, self-advocates, and family members—to improve services for children with or at risk for neurodevelopmental disabilities.

Hoselton learned about LEND through school and saw it as a way to grow as both a self-advocate and advocate for others. "I wanted to learn how I could improve society for people with disabilities using my own lived experience," he explains.

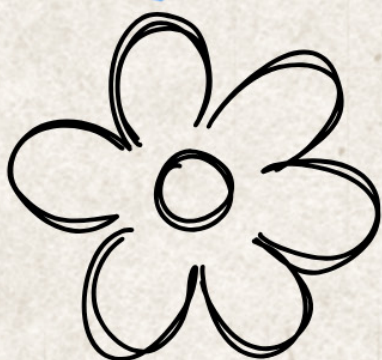
After a year in the program, Hoselton says it's been transformative. "I've gained a lot of knowledge about how people see the world through their experience with a disability," he says. This broader perspective has helped him understand what changes are needed to improve lives.

LEND's interdisciplinary approach allows trainees to learn from each other's expertise. "Working with different disciplines, I've really enjoyed sharing ideas and making connections," Hoselton says. These conversations, he adds, are key to improving processes like diagnosis and treatment for people with disabilities.

Julie Schears, a longtime LEND disability advocacy coordinator, has mentored Hoselton throughout his training. "She's been great. I've enjoyed working with her," he says.

Schears helped Hoselton prepare to speak with Wisconsin legislators during Disability Advocacy Day in 2025. He shared how Medicaid has impacted his life and how cuts could affect his independence, healthcare, and access to services—advocating not just for himself, but for others with disabilities.

Hoselton is considering a career in healthcare and hopes to become a medical assistant. He also plans to continue his advocacy work. "I want to be a long-term advocate and speak at schools and other places to help make society better for people with disabilities," he says. "There's still a lot we need to improve." ■



FINDING CONNECTION:

The struggles and strengths of building relationships for individuals with autism

by Emily Leclerc

Note: Ibrahim and Madelyn expressed that they did not have a preference regarding the type of language they preferred when being referred to. This article uses person-first language throughout.

Relationships are hard. It's part of why there are countless books, podcasts, and blog posts about how to build, maintain, and keep relationships. But even with access to that endless sea of information and advice, building healthy, valuable, and long-lasting relationships, both platonic and romantic, can feel like a herculean task.

Wanting connection, wanting relationships, is a core part of what it means to be human. The drive to foster deep social bonds is inherent in humans. "Human beings have a need and a desire for connection. It is part of how our brains and bodies work. There are physiological and biological responses to building connections that reinforce and reward that behavior," says **Madeline Barger, MS, LMFT, BCBA, CST, lead behavior analyst in the Waisman Center Autism Treatment Program's Teen and Young Adults program**, licensed marriage and family therapist, and AASECT-certified sex therapist. "Everyone needs healthy relationships, deserves them, and has a right to them."

Even with that drive and need, navigating today's social landscape to find friends and partners has a multitude of challenges. For someone who is on the autism spectrum, finding and fostering relationships can be even more complicated. "Sometimes it feels like rocket science," says Ibrahim, an adult with autism who has worked with Barger.

Popular media, like the show "Love on the Spectrum," has started to bring increased awareness to the hurdles that individuals with autism often face when endeavoring to build connections. But even with that new awareness, the road can be long and full of bumps.

FIGURING OUT HOW TO TAKE THE FIRST FEW STEPS

Autism is a developmental disability resulting from differences in how the brain is wired and is characterized by difficulties with social and communication skills and restrictive or repetitive behaviors. Every individual with autism is impacted differently, with a diverse list of symptoms that can range greatly in severity. With social communication being a core area that is affected, autism adds another layer of complexity to the already complex skill of building relationships.

The first big hurdle is access. That is easier for people who are still in school as that grants you access to all of your peers. It is much simpler to start building a friendship with someone you are guaranteed to see every day. Without the regular proximity of peers that occurs when in school, finding places to meet new people and build those relationships can feel almost like a second job. And for individuals with autism, that first step and starting point can feel formidable.

"Time and access, for any adult, whether it is a tired parent, someone living on their own, or someone who just wants to meet people, is a big deal. Like, how do I start this," Barger says. "Where is the space in my life for this? How do I find people that I might be able to and want to connect with? Then you add the idea of disability where there can be a lot of stigma and judgment and then the effort to go make a friend or join a social group becomes even more monumental and heavy."



Madelyn

Figuring out where to go to socialize mixed with the potential risk of judgment, stigma, and rejection can be a paralyzing combination. Being treated poorly because of their differences is unfortunately a reality for many individuals with autism. "I have the lived experience of people not being so kind to me in the past and being outcast," Ibrahim says.

It is impossible to know whether or not someone will be accepted by a new group of friends. The resulting fear and anxiety, that is often reinforced with poor previous experiences, can make entering a new space with unfamiliar people feel incredibly intimidating and challenging. "Many clients have talked to me about worries about being judged and other similar feelings," Barger says. "That doesn't mean there is a lack of interest or desire to socialize, it just means we work on ways to manage that because

being judged by potential friends is upsetting and scary."

There are many different ways to work towards being a little more comfortable and confident entering new spaces. Barger is always the first to say that it is a very individual process and it may take

"How do I find people that I might be able to and want to connect with? Then you add the idea of disability where there can be a lot of stigma and judgment and then the effort to go make a friend or join a social group becomes even more monumental and heavy."

-Madeline Barger, MS, LMFT, BCBA, CST

some time to learn what works for each person. Maybe it is bringing someone else with you. Maybe it's intentionally seeking out a space targeted towards neurodivergent individuals. Maybe it's finding a group focused on a niche interest. Or maybe it's starting first with building online friendships. Meeting people online can be a good option for some as it has lower social demand than interacting with others in person. It can be an

opportunity to build confidence before endeavoring to build in-person relationships. Barger emphasizes that it's important to find what method works best for each person to help them get in the door.

Unfortunately, the fears of judgment and rejection don't always stop after addressing the initial anxiety. Even once a friendship is established, Ibrahim and Madelyn, a young adult with autism who has worked with Barger, continue to be very selective about who they tell about their autism diagnosis. "I still don't tell all of my friends, even the ones that I love. Some of them know this about me, the ones I feel safest with, and some of them don't," Madelyn says. Ibrahim is the same with only a select few people in his life being privy to his diagnosis. The vulnerability in opening up to someone about being on the autism spectrum can be daunting and is not always met with a kind reaction.

FROM SOCIAL BLUEPRINTS TO SELF-CONFIDENCE: BUILDING SKILLS AND RESILIENCE

Compounding everything can also be some of the challenges that individuals with autism face with social skills. Verbal communication is one skill but often where individuals with autism struggle is with the different forms of nonverbal communication and understanding all of the unspoken social rules. "I compare it to – you know in Excel when it will autofill in the rows with numbers? That's neurotypical people's social skills. For my social skills, it's like I have to manually fill in every single number. You can learn but it takes a lot longer and is a lot harder," Madelyn says.

Body language, social cues, social conventions, and unspoken societal social rules can often be more difficult for individuals with autism to follow and interpret. Typically developing individuals often don't realize how much nonverbal communication they are engaging in and responding to during conversations. It becomes an innate skill that plays out almost entirely subconsciously. It can feel like neurotypical individuals have a cheat sheet for all of the unspoken social rules that individuals with autism never got.

This can lead to conversations requiring significantly more thought and energy for individuals with autism as they have to expend extra processing power to keep the rules in mind and interpret the nonverbal communication. Unintentionally or unknowingly breaking the unspoken social rules or misinterpreting nonverbal communication can also play into fears of judgment and rejection.

"I think a big part of friendship is reading body language and picking up on social cues. I've definitely learned some of it but it is still really challenging for me," Ibrahim says. "And people sometimes have this knee-jerk judgmental reaction to me because of it. Then people don't always take the time to get to know me."

Learning and developing these skills is a common area for Barger and the individuals that she works with, including Madelyn and Ibrahim. They will work together to build their own toolbox and guidebook for what they want to do during different interactions and conversations and what social cues and rules to be aware of. The services Barger provides are a part of the larger Autism Treatment Program at the Waisman Center, that serves individuals with autism from preschool to young adulthood.

Barger utilizes a variety of methods to help her clients put together a social toolbox and build confidence in their abilities to handle different social situations. It all depends on what would be most helpful for each individual person. The methods can include talking through how different conversations could go and how they would



Madeline Barger, MS, LMFT, BCBA, CST

want to respond, writing a script or putting together a list of notes, providing examples of how others have communicated during different social interactions, and role-playing.

"There is also almost a social structure that we can lay out for people to fill out as they want," Barger says. "And thankfully over the years it has become less about this is what socializing should look like and more about here is a framework for how to advocate for yourself and you plug in the content you want."

Having to more deliberately learn and work on a variety of social skills has the potential to sometimes lead to individuals with autism and other disabilities having better and more adaptive skills than neurotypical people, Barger says. Needing to consciously spend time thinking about and working on these skills has the benefit of giving individuals more space to improve and develop them in ways that others might not. "Now I almost run circles around neurotypical people when it comes to socializing because I've had so much training from loved ones, Madeline [Barger], and the Waisman Center in adapting to a neurotypical world. I also have spent a lot of time actively thinking about the social choices I make," Madelyn says.

Today, both Ibrahim and Madelyn have built supportive, loving, and deeply valuable networks of people around them. They truly cherish the relationships in their lives and spend a lot of time and energy nurturing their friendships and partnerships. "I don't take my relationships for granted. I am very serious and intentional about them," Madelyn says. "I really care about my friends. Like really care about my friends."

With that depth of care comes a unique ability to genuinely empathize with those around them. They know how hard it can

be to find people to connect with. How hard it can be to suffer unkindness, isolation, and rejection from others. How important it is to strive for inclusion and acceptance. “Nobody deserves to be alone. Everybody deserves to connect with somebody,” Ibrahim says. “Experiencing unkindness and being outcast has convinced me to make sure that I don’t do that to anyone. It has made me a lot more compassionate for people.”

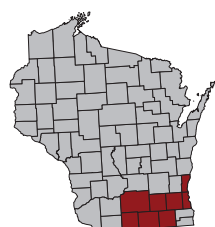
The unfortunate flip side of the coin is that struggles with building relationships and the social challenges individuals with autism face can make them more vulnerable to abuse, manipulation, and intense struggles with relationship loss. Barger says that the best ways to help mitigate those risks is to focus on awareness, prevention strategies, and building resiliency through strong coping strategies. Talking about what signs, behavior patterns, and red flags to be aware of, strategies on how to protect yourself, and how to grieve the loss of a relationship in a healthy way are all ways to help prevent abuse. Barger also works with her clients to intentionally cultivate ways to find joy and happiness outside of their relationships so that if they were to end, it wouldn’t feel as though their entire world has caved in. Resiliency and protection strategies are an equally important part of a social toolkit alongside all of the social skills.

REDEFINING RELATIONSHIPS

There is often this idea that friendships and other types of relationships are supposed to look a certain way. That they should have this specific structure or that particular form of connection. That they should fit into this one specific friendship box. Not only is that limiting but it also devalues the wide diversity of ways relationships can look.

Every person has the right to decide what they want their relationships to look like and how they want to go about cultivating them. Individuals with autism can have a wide variety of needs in their relationships and they have the right to foster the connections that best suit them in whatever form that takes. “The freedom to just be yourself around someone that is accepting of you is an intoxicating and liberating thing,” Madelyn says. There is great beauty in that diversity.

Learning to be open and accepting of different kinds of connection not only benefits individuals with autism but everyone else as well. As long as there is safety and consent, friendships, partnerships, and relationships are yours to build as you please. And their shape is entirely up to you. “Understanding that there are so many ways a friendship or relationship can be is something we should be doing with everyone all the time,” Barger says. “I truly think that the autism community really teaches everybody else how to do that and it is a beautiful thing.” ■



■ SITE TRACKING AREA

Autism by the Numbers:

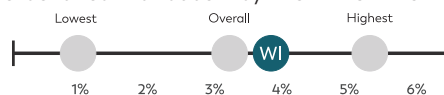
Waisman Center investigator and epidemiologist **Maureen Durkin, PhD, DrPH**, leads the **Wisconsin Surveillance of Autism and Other Developmental Disabilities System (WISADDs)**, one of 16 **Autism and Developmental Disabilities Monitoring** sites that contribute to the CDC’s autism report. The most recent report was released in 2025.

A Snapshot of Autism Spectrum Disorder in

Wisconsin

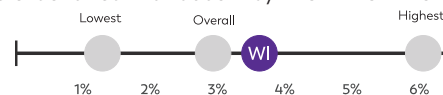
Findings from the Wisconsin Surveillance of Autism and Other Developmental Disabilities System (WISADDs) help us understand more about the number of children with autism. These findings include the characteristics of children with autism, and the earliest age, on average, at which they are evaluated and given a diagnosis.

About **1 in 26** or **3.8%** of **8-year-old** children were identified with autism by WISADDs in 2022.



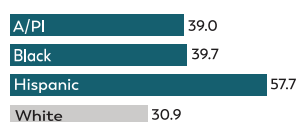
The percentage, in teal, is higher than the overall percentage identified with autism, in gray, (3.2%) in all communities where CDC tracked autism among 8-year-olds in 2022.

About **1 in 28** or **3.6%** of **4-year-old** children were identified with autism by WISADDs in 2022.



The percentage, in purple, is higher than the overall percentage identified with autism, in gray, (2.9%) in all communities where CDC tracked autism among 4-year-olds in 2022.

Among **8-year-olds**, Asian or Pacific Islander (A/PI), Black, and Hispanic children were **more likely** than White children to be identified with autism.



There were no other significant differences in identification between races or ethnicities. Values indicate prevalence per 1000.

Half of **8-year-old** children with autism were diagnosed by a community provider by **43 months** of age.

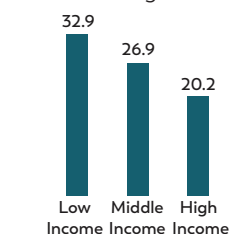
Of 8-year-old children with autism, **52.8%** had a comprehensive developmental evaluation by 3 years of age.



Among **8-year-olds**, boys were **3.2 times as likely** as girls to be identified with autism.



Autism prevalence was higher among **8-year-old** children living in lower-income neighborhoods compared with children living in higher-income neighborhoods.



Values indicate prevalence per 1000.

Transitions



Lisa Marie Carilli McCord, associate director of the Waisman Early Childhood Program (WECP), retired at the end of October after an extraordinary career spanning more than 35 years. As the longest-serving teacher in the program—having joined WECP in 1989—Lisa Marie became not only a beloved educator but a cornerstone of the program’s identity and mission.

Her unwavering passion for early childhood education and her deep love for every child who entered the WECP classrooms have left an enduring legacy. Lisa Marie truly embodied the WECP’s commitment to inclusion and exemplified excellence in education.

Established in 1979 as part of the Waisman Center, the WECP was intentionally designed to ensure that children with disabilities receive high-quality early education in inclusive settings. Up to one-third of the program’s enrollment is reserved for children with disabilities, creating classrooms where all children learn and play together—fostering empathy, understanding, and belonging.

“The mission of inclusion is so important. Every child is unique,” Lisa Marie shared. “Every child should be given the opportunity to grow, learn, and be included.”



Paul White, MA, founder of Community TIES (Training, Intervention, and Evaluation Services) and former director of the Waisman Center’s Community Outreach Wisconsin program, passed away unexpectedly on June 17, 2025.

His life can be distilled to a single concept: he was a consummate infracaninophile—a lover of the underdogs. He made everyone a friend, treated everyone with respect, and saw value in everyone. And he lived his life with humor, love, and above all, a smile on his face. He was a visionary who helped redefine what it means to support individuals with intellectual and developmental disabilities (IDD) in living full, meaningful lives within their communities. Paul built TIES from the ground up, crafting individualized behavioral support plans that honored each person’s unique needs, strengths, and circumstances. His approach was holistic, involving families, caregivers, healthcare providers, and community members.

He believed that challenging behaviors were often expressions of unmet needs—and he worked tirelessly to meet those needs with empathy, skill, and respect.

Under Paul’s leadership, TIES expanded to include psychiatric care, crisis response services, and community training programs. He helped establish safe houses for individuals in behavioral crisis, ensuring they received support—not punishment. His training programs, like Managing Threatening Confrontations, empowered schools, community agencies, and even international partners to adopt more compassionate and effective practices.

His work changed lives, and his spirit continues to guide those who carry his mission forward.



Danielle Gerber and Cara Coleman giving a FLAG presentation at the UW-Madison School of Medicine and Public Health.



Family-Led Academic Grand (FLAG) Rounds:

Family stories as a tool for teaching patient and family-centered care to medical trainees

by Charlene N. Rivera-Bonet

The lecture took place in an auditorium full of pediatric medical trainees, and attendings, but Cara Coleman transported everyone in the audience into a clinic waiting room with her, her daughter Justice, and the receptionist. With specific and very intentional details, she described her surroundings, her thoughts, emotions, her daughter's distress, and the conversation that went on the morning she experienced one of many instances of ableism in the pediatric care of her daughter. "Can't you just change her and do that stuff on the floor in the open bathroom?" the stern receptionist asked. Eight-year-old Justice, who had congenital anomalies that led to multiple disabilities and complex medical needs, was there for a long-awaited appointment, which was running 40 minutes behind. She needed to be catheterized and changed.

The receptionist's solutions were for Coleman to lay Justice down on the bathroom floor in the lobby of a major children's hospital or take her home – neither a reasonable solution. Coleman said she could change her in the trunk of her car but that would be a minimum of 45 minutes. What if they got called? "Well, then, you miss your appointment," was the answer she was met with. Coleman and Justice decided to wait.

After narrating this instance of ableism – discrimination or prejudice against individuals with disabilities – Coleman brought everyone back from that hospital waiting room and into the auditorium again. Her and Justice's story set the foundation for the discussion that followed: expectations, legal standards, and the American Disability Act in pediatric health care of children with complex medical needs.

This was the first of five **Family-Led Academic Grand (FLAG) Rounds**, national, quarterly educational sessions done in collaboration between the **University Center for Excellence in Developmental Disabilities (UCEDD)** at the Waisman Center, the Department of Pediatrics at UW-Madison, and the Bluebird Way Foundation. FLAG Rounds were developed by Coleman and **Danielle Gerber** to use family faculty, or family members of children with complex medical needs as lecturers, and storytelling as a strategy to develop the knowledge, skills, and attitude in medical students and providers to dismantle ableism in pediatric care and partner with families in the care of their children. Each round is presented by 2-3 different family faculty, starting with their stories, and ending with their lessons.



Family faculty and storytelling are key parts of FLAG Rounds. “Having family faculty lead grand rounds sort of turns grand rounds on its head a bit in terms of what the usual expectation is and that’s very unique,” says Heidi Kloster, MD, associate professor in

the Department of Pediatrics and FLAG Rounds advisor. Medical grand rounds are a formal method of medical education in the form of meetings in which healthcare professionals discuss and learn about clinical information. In FLAG Rounds, family members of children with medical complexity are the experts. “The heart of FLAG Rounds is using family stories,” Coleman says. They wanted to use an already established system and flip it a bit to expand the role of families in medical education.

“I think it is a humbling experience because we get too used to, in a medical training situation, just learning from peers and those that may be hierarchically above us when there’s great teachers in every level of what we experience,” says Rachel Streckert, MD, pediatric chief resident in the Department of Pediatrics at UW-Madison who works in complex care and attended FLAG Rounds.

Coleman and Gerber, who is a family engagement specialist in the UCEDD, share a passion for patient and family-led care. This is an innovative approach that involves providers collaborating with patients and families at all levels of healthcare, and “understanding that our patients and families bring with them lived experience and expertise and knowledge that is just as important as the expertise and knowledge of the clinical care,” says Darcel Jackson, FLAG Rounds family faculty.

During the first FLAG Rounds, Gerber followed Coleman in sharing her experience with her son Jack, who was born with a genetic condition that caused intractable epilepsy and developmental disability. She narrated a day when Jack was having a “straight-forward” procedure to remove a mass from his chest. Five hours after what was supposed to be a 2-hour procedure, Gerber and her husband were paged. Everyone in the auditorium was transported into the PACU (post anesthesia care unit) where the Gerbers stood next to four-year-old Jack’s bed, with all the medical equipment beeping. Jack was in pain and his parents could see this, but no one else could. The anesthesiologist was so focused on getting his oxygen levels under control, he could not hear Gerber repeatedly say that Jack was in pain.

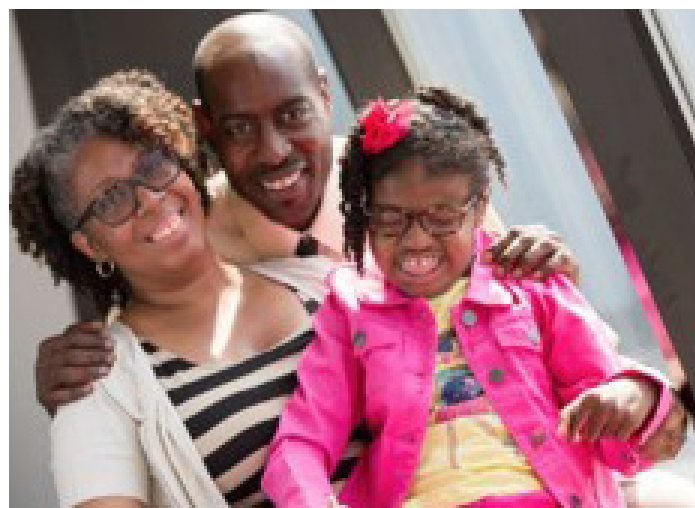
She pressed. “We can’t force that [bipap] mask on him when he is like this, it will only distress him more,” Gerber narrated. The doctor insisted that he had already given him pain medication and his priority was to get his breathing under control. It was protocol, he stated. “I don’t see your child showing the type of pain response that would indicate that he is in pain to the extent that I would alter protocol.” Gerber spoke up. She knew Jack was in pain and his breathing wasn’t going to be controlled until that was addressed. After a few rounds of pain medication, his breathing stabilized.

Back at the auditorium, Gerber went on to talk about the lessons to learn from her and Jack’s story. After Jack’s passing in 2020, Gerber spent a lot of time thinking about what went well with his healthcare and why, and what could she do with that knowledge. She developed a passion for medical education, and after training through the **Leadership Education in Neurodevelopmental and Related Disabilities Program** at the Waisman Center, she started work designing curriculum for medical education that included lived experiences from her and many other families.

Coleman was very familiar with the power of storytelling. She wrote a children’s book about her daughter called “I am Justice, Hear me Roar!” which she and her daughter used to educate others about disability and inclusion. Stories “connects us as humans,” she says. For Gerber “stories have a way of making you feel things, and the hope is that when you feel something, you’re able to take a moment to reflect on what you are feeling and why. So then pairing that with a strategy [for family-centered care], that’s the heart of what we’re trying to do with FLAG Rounds,” Gerber says.

In order for these stories to be effective in delivering a medical lesson, family faculty go through months of training in medical education competency. “Cara and Danielle have designed their curriculum for the family faculty in such a way that they have a deeper understanding of the training that medical providers go through, and that, I think, lends itself well to allowing them to craft stories and teaching points that really hit home,” Heidi Kloster says.

“This is the first time that I’ve been in a role that does that capacity



Jackson family



June and Lisa

building for the family advisors to understand the perspective of the residents and medical providers and the education they go through including how the education system can be dehumanizing to the providers. So that was really neat to establish some common ground there,” says Lisa Treleven, FLAG Rounds family faculty.

Treleven shared her and her daughter Juniper’s “June” story during the second FLAG Round, under the topic of “Say What? Language Matters.” June who is 11 years old, is medically complex with a tracheostomy, heart condition, epilepsy, and an undiagnosed genetic condition.

Treleven has experience with advocacy and advisory roles giving the patient/family perspective to entities that are involved in health care. She is no stranger to teaching and advocacy, and unfortunately, no stranger to ableism. During FLAG Rounds, Treleven and two other family faculty shared their stories and the lessons to be learned from them regarding the importance of language in the care of children with medical complexity. Each story shared took months to develop.

Each group of family faculty had a writing coach that helped them get their story down to the right length and the right tone. They also had to think about how to integrate the competencies and teaching points required to make it a grand round. “There was a lot of editing and a lot of group work to shape these stories,” Treleven explains.

For Darcel Jackson, this process really helped her feel more confident that the story would resonate and land well with a larger crowd, specially a story in which she had to be vulnerable.

Jackson’s FLAG Round was entitled “The Compass We Carry.” It included stories from three families that involve diagnostic overshadowing, end-of-life decision making, and defining dignity and share strategies around uncertainty to ensure alignment between families and providers.

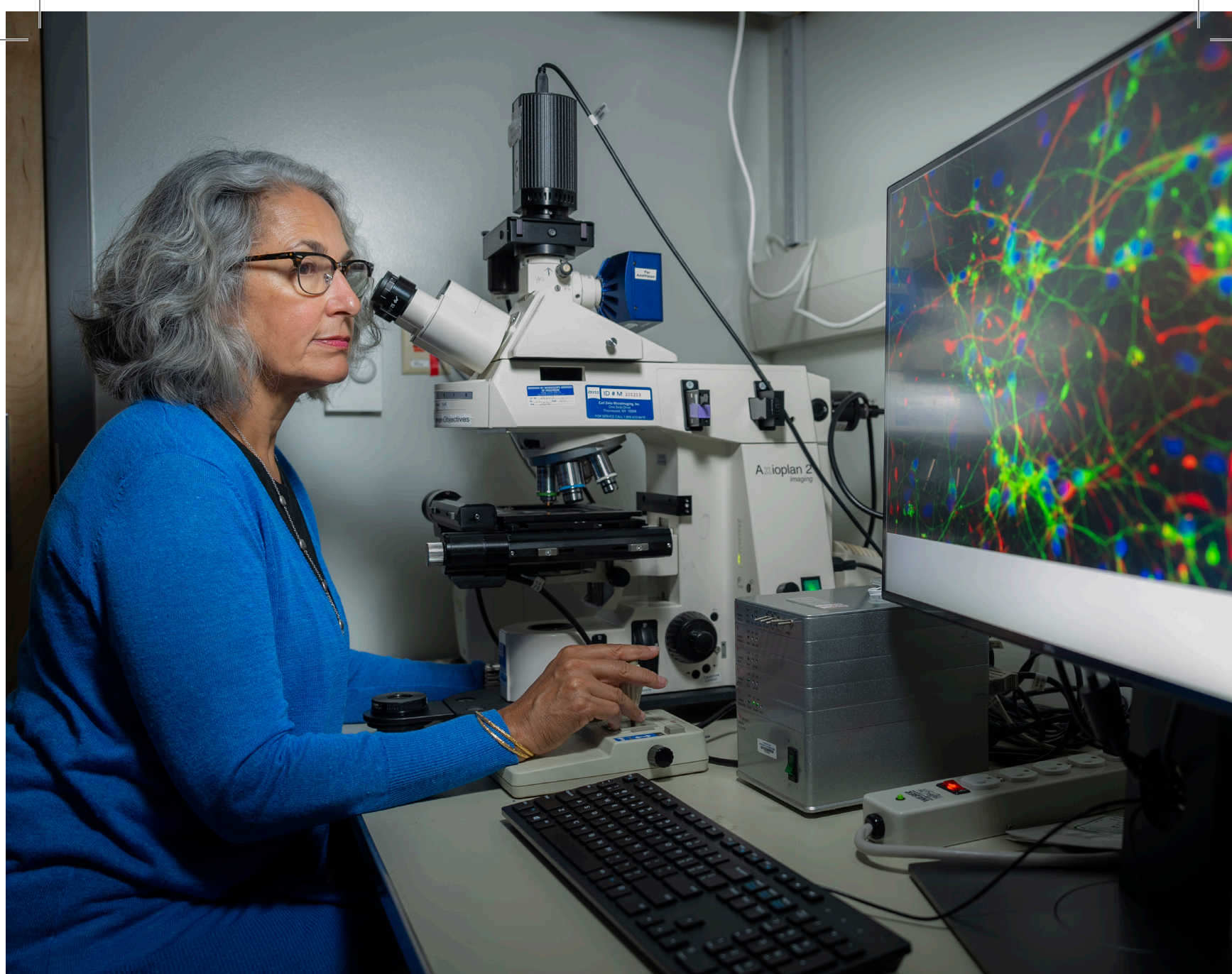
For 18 years, Jackson and her family navigated a journey of the unknown with her daughter Anniyah, who was born with mosaicism for trisomy 8 and 18, two rare chromosome abnormalities that impacted her full body system and organs. Something they knew for sure, is they wanted her to have a great quality of life.

During her lecture, Jackson talked about her experience having end-of-life conversations with her daughter’s providers. “I think for me, how it ties into ‘The Compass We Carry’ is that families and medical teams may not always be heading in the same direction. [Everyone] wants the best outcomes. But the best outcome may not look the same,” Jackson says. “For us as a family, the best outcome wasn’t keeping her alive year after year after year, totally dependent on technology and on equipment for survival, if we were going to be losing her ability to smile, we’re going to be losing her ability to be aware of the world around her and interact.”

Jackson’s hope is that everyone who attends FLAG Rounds leaves recognizing that family expertise is needed and important, and that families are an integral part of the care team. “I believe our lived experience is also clinical experience, and so the more that our clinicians themselves understand that, the more they’ll hopefully see that we are an equal part of the care team,” Jackson explains.

Treleven hopes that clinicians will see the common grounds with families when it comes to the medical world. “My hope is that it will be humanizing for patients and families. That it will give [providers] that lens to see through and hopefully connect to their own experience too. That in the same way the healthcare education and system can be dehumanizing to providers and it’s a challenging environment for them...it’s challenging in those same ways for patients and families, and that we can partner together to shape the system.”

For Kloster, ableism arises when people are in situations they don’t understand or make them uncomfortable, and instead of leaning into the discomfort they lean away, contributing to treating the children and families in a way that is ableist. “And what I hope that FLAG Rounds will do is increase awareness of how impactful and painful those experiences are and how much they detract from the care that we’re able to provide our patients.” ■



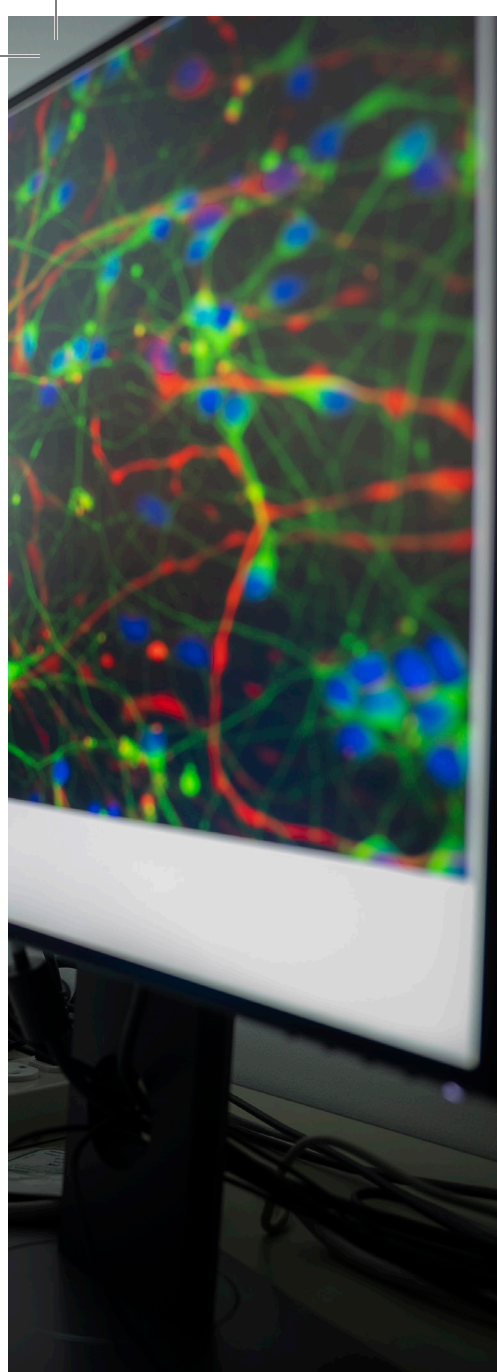
Anita Bhattacharyya, PhD

Waisman researchers reveal early metabolic dysregulation in neurons as possible trigger for neurodegeneration in Down syndrome

by Emily Leclerc and Charlene N. Rivera-Bonet

In a new discovery, researchers at the University of Wisconsin-Madison have identified a potential early trigger for neurodegeneration in individuals with Down syndrome – dysregulated energy metabolism in neurons from birth. It offers new hope for possible future treatments that may delay the onset of Alzheimer's disease through targeted early intervention.

The lab of Waisman investigator **Anita Bhattacharyya, PhD**, associate professor of cell and regenerative biology at UW-Madison, found gene expression signatures that indicate energy metabolism was dysregulated in neurons in individuals with Down syndrome since birth. Their recently published research, the first ever to sequence the genes of human basal forebrain cholinergic neurons, sought to find early drivers of neurodegeneration that could serve as potential therapeutic targets to delay neurodegeneration and cognitive decline in individuals with Down syndrome.



Nearly all individuals with Down syndrome develop Alzheimer's disease (AD). Unlike the general population, neurons of individuals with Down syndrome start showing signs of degeneration very early on, even before cognitive impairment becomes apparent. "We know [the neurons] degenerate, but we don't know what's driving that," says **Nicole West**, a graduate student in the Bhattacharyya lab and first author of the study. Typically, some of the first neurons to degenerate, and the ones West and Bhattacharyya focused on, are in the basal forebrain. This area regulates learning, memory, and attention and its loss of neurons is believed to be an early driver of cognitive decline associated with age and AD. Researchers have found that deterioration of the basal forebrain neurons can be seen decades before the onset of Alzheimer's symptoms, indicating that something must be making them susceptible to early degeneration.

West, Bhattacharyya, and the collaborating labs of Waisman investigators **Andre Sousa, PhD**, assistant professor of neuroscience at UW-Madison and **Daifeng Wang, PhD**, professor of biostatistics and medical informatics and computer sciences at UW-Madison, performed single-cell sequencing of basal forebrain neurons in postmortem brain tissue of young individuals with and without Down syndrome, ages 0-2 years old. "Researchers have only looked at these neurons once they are already dysfunctional and dying," West says in explanation of why they chose to look at younger individuals. "You can't really gather a whole lot at that point about what is contributing to the degeneration."

Analysis revealed that as early as birth, neurons in the basal forebrain show dysregulated energy metabolism that may cause the cells to experience higher levels of oxidative stress. This can lead to DNA damage, protein degradation, and overall cellular

damage that makes them susceptible to degeneration and cell death. "We didn't expect to see this kind of cellular dysregulation this early in life," West says. "Again, these neurons degenerate decades later so I was very surprised to see that at birth these neurons are already dysfunctional."

They also saw markers for neuroinflammation and deficits in the neurons' myelination, which is a coating around the neurons that enables faster and more efficient communication. "None of these changes were subtle," Bhattacharyya says. "We were surprised at just how striking the results were."

Even as this discovery reveals important information it also shows how much there is left to unpack. Metabolism can be difficult to study so it will take time to fully unravel the extent of the dysregulation, what genes are contributing, if other cell types are being impacted, and how researchers might start thinking about using this knowledge to develop new therapeutics.

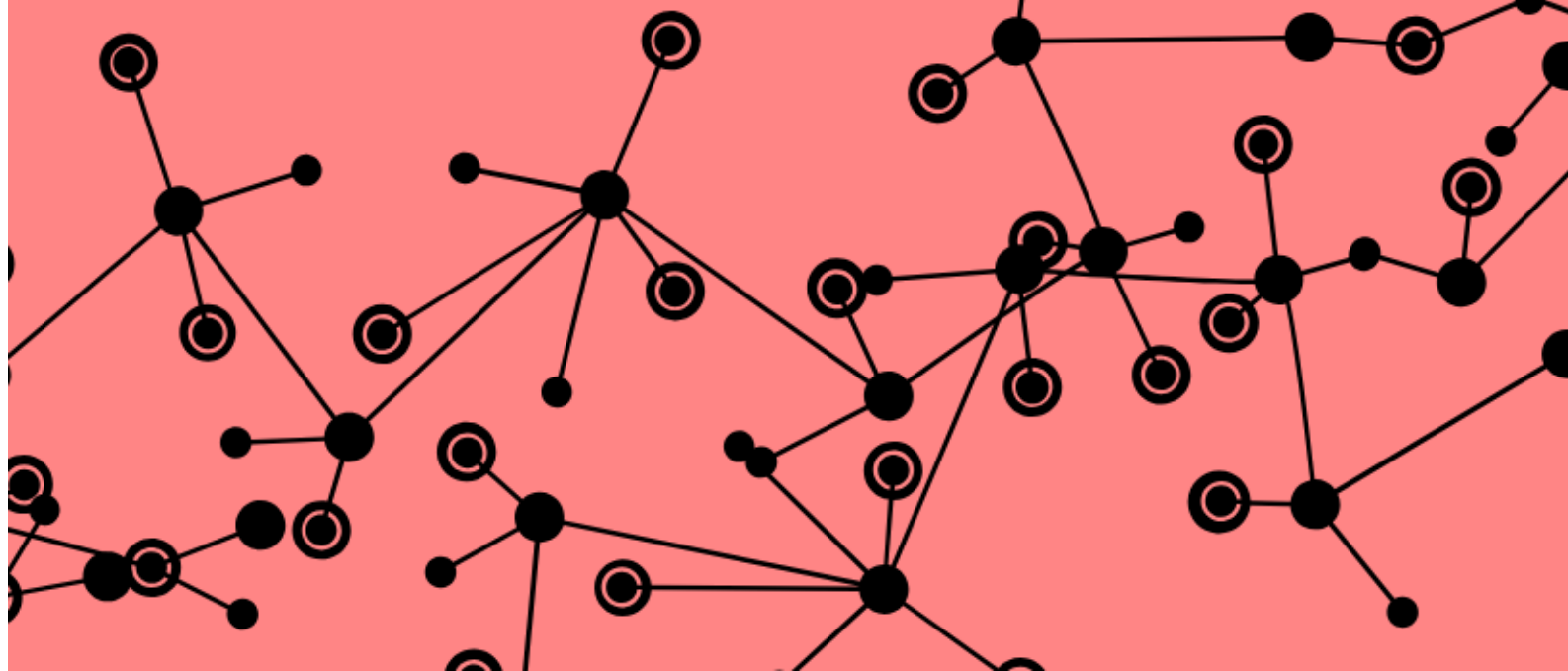
Finding how early the dysregulation starts presents opportunity for future therapies as well. "We went in looking for early things that could be driving this degeneration and that could be therapeutic targets," West says. "At this early point in someone's life the neurons are still healthy enough that if a therapeutic is used it has the potential to delay the degeneration of these neurons and the cognitive decline."

While this research is a long way from putting together new treatments for Alzheimer's and Down syndrome, it gives researchers another layer of important knowledge on the path toward effective treatment development. ■

This research was supported by the National Institutes of Health, the National Institute on Aging, the Medical Scientist Training Program T32, the Ruth L. Kirschstein Individual Predoctoral NRSA from the National Institutes of Health, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Additional funding came from the University of Wisconsin-Madison Sophomore Research Fellowship, the Brain Research Foundation, the William F. Vilas Trust Estate Award, Wisconsin Alzheimer's Disease Research Center Research Education Component Award, and the Wisconsin Partnership Program New Investigator Award from the University of Wisconsin-Madison.

Meet ARTEMIS: The new AI helping researchers reconstruct the hidden stories of cell development

by Emily Leclerc



Building a complete developmental trajectory of cells is close to impossible with today's technology, but new technology developed at the Waisman Center is taking scientists a step closer to achieving it. Machine learning, a form of artificial intelligence,



Daifeng Wang, PhD

can step in to help fill in the gaps. The lab of Waisman investigator **Daifeng Wang, PhD**, associate professor of biostatistics and medical informatics at UW-Madison, built a new machine learning algorithm that is able to extrapolate continuous changes in cell populations over time to give researchers deeper insight into cellular processes. The algorithm may enable a more nuanced understanding of cellular development possibly revealing

how conditions like intellectual and developmental disabilities impact cells and brain development at the molecular level.

Cells are constantly in a state of flux and with current data collection methods, it is essentially impossible to accurately capture a continuous measurement of cellular change over time. "Cells are not static. Their change is dynamic and continuous. But the measures researchers take are static. They're like a snapshot of that one moment in time," says Wang. "It's impossible to track something like gene expression in real time across so many cells and so many genes."

Researchers can capture a series of snapshots that give an overall idea of how cells are changing but all of the information in between data collection points is lost. This is where machine learning can play a pivotal role in scientific research.

Wang and **Sayali Anil Alatkhar**, graduate student in Wang's lab and first author on the paper, designed a new machine learning algorithm named **ARTEMIS** (trAjectory infeRence wiTH unbalancEd dynaMic optImal tranSPort) that is capable of taking existing data sets and predicting the missing information in between the data collection time points. The paper outlining the new machine learning algorithm was accepted to the proceedings of the International Conference on Intelligent Systems for Molecular Biology (ISMB) and was published in the journal *Oxford Bioinformatics*. ISMB is the flagship annual meeting of the International Society for Computational Biology. This conference is highly competitive and Wang and Alatkhar's paper is one of very few that have been accepted across the entirety of UW-Madison over many years.

"Say you originally have gene expression data for 1000 cells at three time points from a particular developmental process," Wang says. "Using ARTEMIS we can predict or recover the gene expression across all of the time points in between the three in the data set. It outputs continuous dynamic data across the entire process."



ARTEMIS combines two different machine learning methods in order to generate its output. The first is a variational autoencoder or VAE. VAEs were designed to reconstruct data. “These autoencoders essentially take huge data sets and create a small, compressed representation that is more easily used for data analysis,” Alatar says. The second is a Schrodinger bridge. Schrodinger bridges are another type of algorithm that can help predict continuous trajectories from data it is fed. So together, ARTEMIS’ VAE creates a compressed version of a large data set. Then the Schrodinger bridge predicts a continuous trajectory from the compressed version and lastly the VAE reconstructs and decompresses the data. This leaves the user with a predicted continuous look at whichever process was being studied.

“You can think of ARTEMIS as similar to those things that predict what you will look like when you get older. It connects many images of someone’s face, makes simpler representations of them, and then uses those versions to predict what you will look like in the future,” Wang says. “Our version does that with gene expression rather than pictures.”

ARTEMIS was trained and tested on several real-world data sets including pancreatic cancer cell differentiation and the embryonic development of zebra fish and showed it was able to outperform current methods for predicting lost time point data.

The data sets ARTEMIS trained on were all gene expression data, but the model can handle a variety of data types. “The model is general,” Wang says. “It can easily be applied to any developmental data such as brain development. We can even apply it to typical brain development versus atypical to see how they compare and differ.”

Wang and Alatar also see ARTEMIS’ potential for handling a variety of different cell characteristics as well. Gene expression is just one characteristic. They want to explore ARTEMIS’ accuracy at predicting protein expression, chromatin accessible regions, cell population changes, and more. “We want to explore multimodal trajectories too. Where we can see how two different characteristics are evolving at the same time,” Alatar says.

ARTEMIS’s capabilities give researchers so many new potential opportunities to gain better understandings of cell development across a variety of scenarios. It could help researchers look at changes in gene expression during the development of cells with Down syndrome or reveal what continuous brain development looks like at the molecular level for cells with known genetic causes of autism. It has the potential to be a real asset in the study of intellectual and developmental disabilities, which is generating various time-course datasets. ■

Funding for this research comes from the Simons Foundation Autism Research Initiative, the National Institutes of Health NICHD, HHS, and the National Science Foundation.

Guiding Families Forward:

How the Waisman Center helps families navigate next steps in caring for a child with disabilities

by Emily Leclerc



Moving to a new city can be difficult and overwhelming. Everything is unfamiliar. Even getting to the grocery store can be challenging when trying to navigate unknown streets for the first time. This is where having a GPS comes in handy. Just type in the destination and that automated voice takes you directly where you want to go. Getting lost is a thing of the past. But for families with kids with disabilities trying to navigate how and where to find the best resources and supports for their child, it can feel like trying to drive through a brand-new city with no GPS.

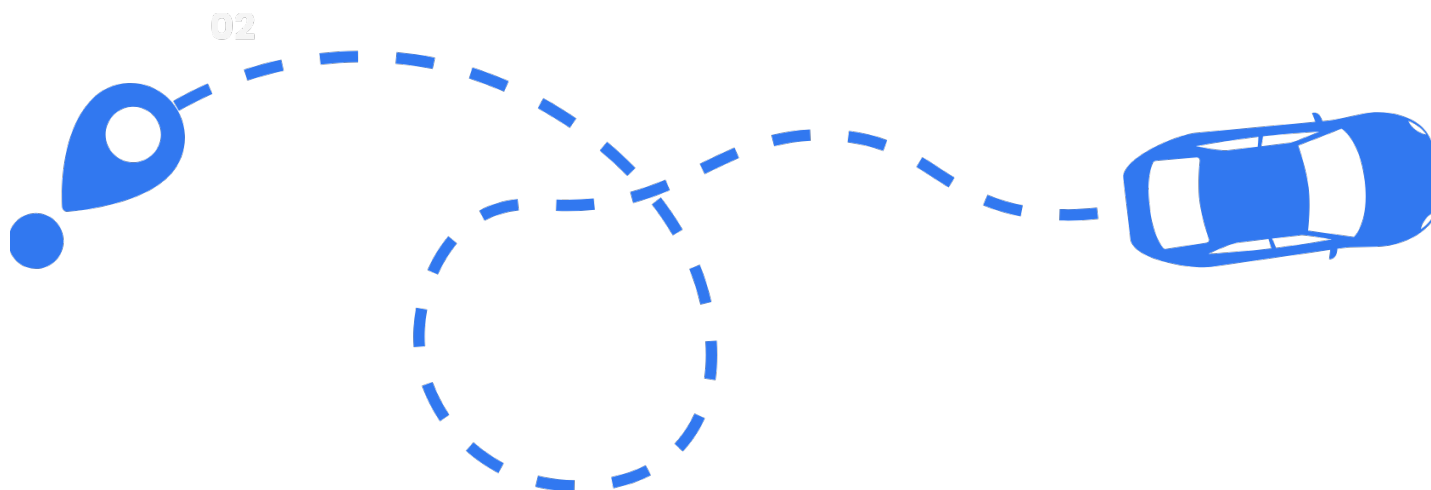
The Waisman Center's team of resource guides and family navigators can help fill in as a GPS of sorts for families and guide them towards the resources that they need. "It is all about partnering with families. We listen to where they are at and where they want to go. It's all about letting them know that we

are on their team and we want to help them connect to whatever resources they are looking for," says Lisa Koob, MSW, social worker, resource guide in the **Children's Resource Center – South**, and family navigator in the Waisman Center's **Autism and Developmental Disabilities Clinic (A&DD)**.

A PHONE CALL CAN MAKE ALL THE DIFFERENCE

Families are able to get support and resources from the Waisman Center through several different avenues. The one that is most accessible is the **Children's Resource Center – South (CRC-South)**. They are always just a phone call or email away.

The CRC-South, which is a part of the Waisman Center's **University Center for Excellence in Developmental Disabilities (UCEDD)**, is one of five resource centers in Wisconsin that serve families of children from birth to age



21 with disabilities and special health care needs. They work with families to provide supportive listening, information, and resources related to their needs and concerns. The center covers 14 counties in south and southwestern Wisconsin, with the rest of the state divided up among the other four resource centers. If the CRC-South gets a call or a message from someone outside of the counties they serve, they will happily redirect and connect them with the CRC-South that serves the county they live in.

The resource guides within the CRC-South support families wherever they are in their journey—whether it be early on as they navigate a new diagnosis or later in their journey as they look for resources before adulthood. The CRC-South has a phone line and email address people can call in or message with a question. Whether the family is looking for an autism evaluation or wondering where to find mental health services or resources to encourage independence, the resource guides can help direct them to information and resources to meet their needs.

“There is so much information out there and the landscape of services and which services take which insurances changes so frequently that for families, I think there’s real value in being able to call someone who can give you a personalized menu of resources,” says **Erin Thomson, MSW, LCSW**, clinic coordinator of the A&DD Clinic and Waisman’s Newborn Follow-up Clinic, licensed clinical social worker. Thomson is also a family navigator in the A&DD Clinic. “Anyone can go to Google, we don’t have secret resources, but we can tell you exactly what places take your insurance and provide the service you are looking for without you having to call a thousand different places.”

The resource guides take the time to listen to the family’s concerns and questions to understand what they need and the best ways to get them access to it. “I’ll answer their initial question and then also do a little investigating to make sure that the family is connected to all of the things that they should

be,” says **Amy Lyle, MSSW**, social worker, resource guide in the CRC-South, clinic coordinator in the Down Syndrome Clinic, and a family navigator in the A&DD Clinic. “We want to make sure we’re not missing anything and they know about everything that is available to them. Our calls are never quick!” The CRC-South’s phone line is also not just limited to families. Case managers, caregivers, clinicians, school staff, or anyone else is welcome to call and ask a question about disability resources and services.

DEMYSTIFYING THE CLINIC JOURNEY AND HELPING LAY A PATH FORWARD

While the CRC-South is an open resource to the counties it serves, it was intentionally integrated into the Waisman Center to ensure that families visiting any of the center’s ten specialty clinics have direct access to its services. For those who come through the clinics that live in counties outside of the CRC-South’s reach, they will be connected with the resource center

that serves the county they live in. Caring for a child with a disability or special health care needs often involves navigating a complex web of clinicians, therapies, and support systems. By keeping the CRC-South closely connected to the clinics, families always have a trusted place to turn for guidance, questions, and resources tailored to their needs.

In addition to the CRC-South, each Waisman clinic employs dedicated professionals – such as social workers, family navigators, or similar roles – to support families throughout their clinic experience and help ensure that every family leaves with a clearer path forward and the tools they need to support their child’s development and well-being.

LISTENING AND UNDERSTANDING IS A HUGE PART OF THE JOB

One of the hardest parts of the job is when there just aren’t resources available that can meet a family’s needs. “Sometimes the resources just aren’t there. I’ll be working with a family who

“The families can feel like they’re not alone. There is somebody who can listen to them, somebody with a lot of experience helping other families.”
-Aracely Portillo, resource guide

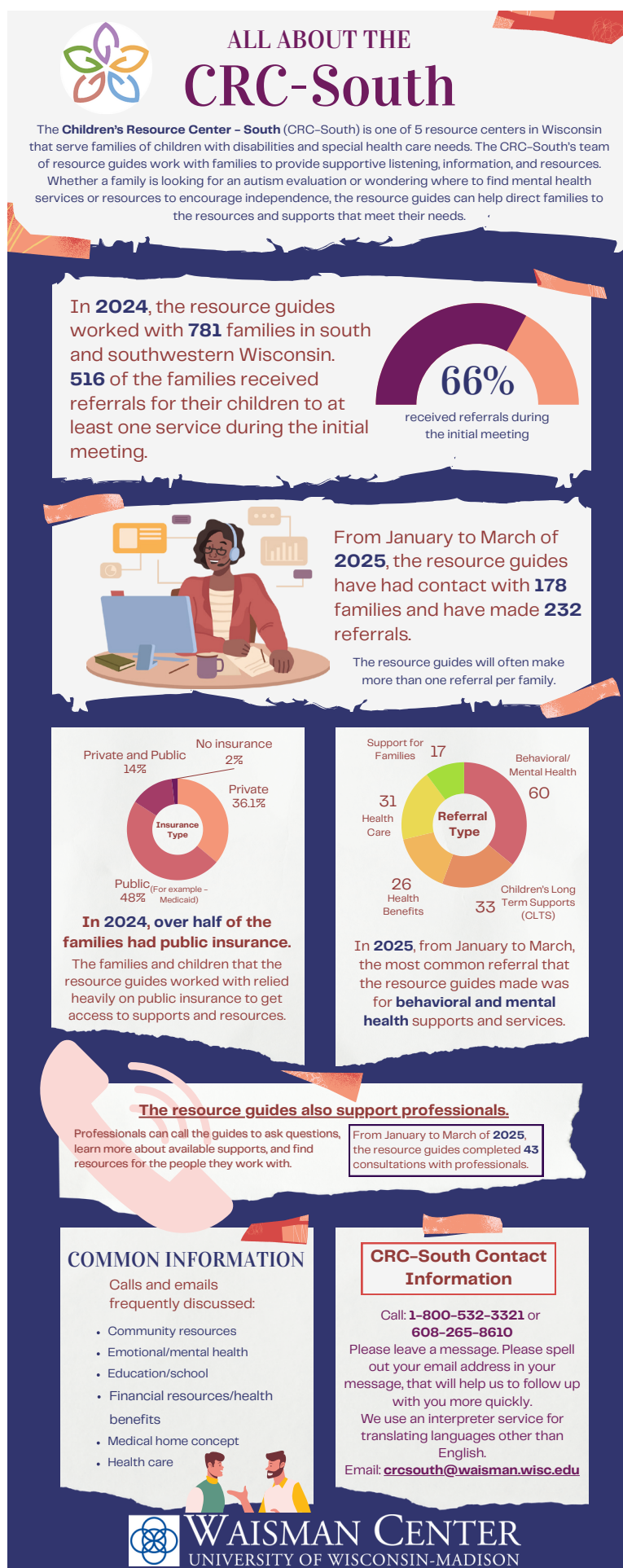
is having a really hard time with their kiddo and trying to find supports but they just keep running into barriers. We do our best to find something and work together during our daily family navigation huddle but sometimes there just isn't anything and that is very hard," says **Lynn Havemann, MEd**, family navigator in the A&DD Clinic and resource guide in the CRC-South.

Sometimes all they can offer is a listening ear and emotional validation, which can be almost as meaningful as a resource or service. "Families are often surprised that somebody calls them right back. They are often calling and leaving a message in both the CRC-South and the clinics and they are always so happy that someone cares enough to respond," says **Meredith Vitaoli, APSW, IMH-E**, social worker and director of the CRC-South. "And even beyond that, the emotional support our resource guides can provide is so important. Families are always incredibly thankful for the time we take in our interactions with them. Our guides always want to hear a family's story and will always take the time to stop and listen and show that they care."

Having someone stop and take a few moments to really listen and validate your experience can be a profound moment. The resource guides and family navigators can sometimes be the emotional support that a family needs during a hard moment. "The families can feel like they're not alone. There is somebody who can listen to them, somebody with a lot of experience helping other families. They know the door they are knocking on is open and someone will always welcome them in," says **Aracely Portillo**, resource guide for the CRC-South.

For the resource guides, family navigators, and clinic faculty, being invited in to take part in even a small part of a family's journey is an incredible honor. They want nothing more than for the entire family to thrive, and being able to use their knowledge and expertise to help is a real joy. Every member of the resource guide and family navigation team at Waisman says they've found their purpose in this job and will be committed to helping families as long as they possibly can be.

"Families can so easily get lost in the system. There's really nobody out there helping guide families to what they need, in terms of the disability service system. We have a really specialized knowledge so we try our best to not let families fall through the cracks by helping them get connected and have at least some level of support," says **Michelle Schumacher, MSSW**, social worker and family navigator in the A&DD Clinic. "Families so often call us and ask where do we go from here. We want to be that touch point for resources and help them find what they are looking for and feel a little less overwhelmed and alone." ■





Waisman Center University Center for Excellence in Developmental Disabilities (UCEDD) By the Numbers – FY 2024



The UCEDD supports the full inclusion and self-determination of people with intellectual and developmental disabilities and their families.

Leveraged nearly
\$9 million
with core funding from the
Administration on
Intellectual and
Developmental Disabilities



That's a return of almost
\$15
per dollar of funding



Provided model services to **5,250** youth,
children, and adults including **8,307** clinical visits



27 grants, contracts, and fee-for-service agreements from
federal, state, and local organizations

Assisted **119** agencies and organizations
that serve individuals with disabilities with

601 hours of technical assistance, con-
sultation, and coaching to improve outcomes,
services, management or policies



Trained **8,857**
people from across
Wisconsin

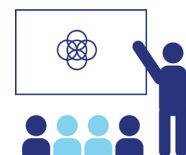
Provided information and referral services
to more than **1,000** families



Trained **86** interdisciplinary LEND
students from **13** disciplines,
177 medical students, residents,
and fellows



Hosted **53** continuing education &
community trainings with more than
2,325 participants



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**“The greatness of a community is most accurately measured by the
compassionate actions of its members.”**

— Coretta Scott King

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Children in the **Waisman Early Childhood Program (WECP)** made a Bucky in celebration of Day of the Badger. The WECP is a model inclusive early childhood program with a developmentally diverse enrollment.

