From the bench to the bedside and back: Improving children's mental health with translational research: An interview with Nakul Aggarwal, MD, PhD

June 4, 2025

Nakul Aggarwal/Photo from SMPH

By Jennifer Bal

Nakul Aggarwal recently graduated from the Medical Scientist Training Program (MD-PhD) at the University of Wisconsin—Madison. He earned his PhD in Neuroscience under the mentorship of Dr. Ned Kalin in the Department of Psychiatry. His graduate work involved cross-species, translational studies in nonhuman primates (NHPs) and preadolescent children focused on elucidating the neurobiological correlates of early-life anxiety. Nakul will be starting a research track psychiatry residency at Stanford University this summer, with plans to specialize in child and adolescent psychiatry.

Nakul is the 2024-25 Americans for Medical Progress /American College of Neuropsychopharmacology Biomedical Research Awareness Day (BRAD) Fellow. He reached out to me to partner with the Wisconsin National Primate Research Center and to spread the word about Biomedical Research Awareness Day, also known as BRAD, which falls on the 3rd Thursday of April each year.

Together we participated in the UW—Madison Science Expeditions at the Primate Center, hosting an exploration station, which brought in over 300 guests, a new center record. Nakul talked with the public about BRAD, the importance of biomedical research and human health, as well as his research experience with NHPs. Read below to learn about Nakul's journey in the MD-PhD program, his cross-species research in translational neuroscience and biological psychiatry, his efforts in science communication, and his advice for students considering biomedical research.

Q: Talk about your academic journey. Why are you a research scientist and a doctor?

A: I was fortunate to grow up in a home that prioritized learning and education. My parents encouraged me to explore new ideas, and I had outstanding teachers who facilitated that pursuit. Specifically, I loved math, biology, and psychology courses in high school.

I started college – at the University of Minnesota – knowing I wanted to study the brain. Early on, I had the opportunity to join a neurology lab that focused on developing deep brain stimulation therapies for Parkinson's disease. This experience was pivotal in my career trajectory. There was a thrill in working collaboratively with people with so many unique skillsets, in designing experiments to uncover the mysteries of the brain, to acquire knowledge that could help people improve their quality of life. It was exhilarating and I was hooked.

At the same time, I got exposure to patient care and clinical research at the county hospital. The two experiences together provided incredible insight into the process of bringing innovations at the bench to patients at the bedside and led me naturally to the physician-scientist path. I enrolled in the Medical Scientist Training Program (MD-PhD) at UW—Madison and cherished my time as I became immersed in translational research focused on childhood mental health, grew as a clinician and researcher, and prepared for a career in child psychiatry.

Q: How did you get involved in primate research? What is your research about and how does it translate to human health?

A: In my sophomore year at the University of Minnesota, I worked at the Neuromodulation Research Center in the Department of Neurology, where for the remainder of my college career I developed and tested a task apparatus to assess the utility of a novel deep brain stimulation paradigm for Parkinson's disease in rhesus macaques. This experience propelled me into my current position as an MD-PhD student in the Department of Psychiatry at UW-Madison, where I spent the past seven years conducting cross-species translational work focused on how early-life brain development relates to pathological anxiety in childhood in rhesus macaques and preadolescent children.

Our work aims to understand how changes in the structural connections between different brain regions might be related to high levels of anxiety. One of the ideas I'm specifically interested in is how changes in myelin, the sheaths of fat that insulate and optimize communication among neurons, may be linked to anxiety.

The studies are highly translatable because nonhuman primates and humans share very similar brain structure, function, and socioemotional behaviors. We've investigated ways to modulate structural connectivity and myelin in the brain and to alleviate maladaptive anxious behaviors, which may one day lead to new, more effective therapies for children with anxiety disorders. In this regard, translational work in animal models is a critical step in the development of novel treatments for any human disease. It can afford us the opportunity to modulate systems that may be mechanistically involved in causing disease and, for example in our lab, test new strategies to prevent and treat childhood anxiety.

Q: When did you learn about BRAD and why did you want to become a BRAD fellow?

A: BRAD is an initiative of the Americans for Medical Progress. The BRAD Fellowship is jointly sponsored by AMP and the American College of Neuropsychopharmacology (ACNP). I first learned about BRAD while attending the annual ACNP conference a few years ago. I became more familiar with the fellowship when two of my colleagues participated in the program and was impressed by the impacts they made through their fellowship projects.

I pursued the fellowship because my experiences in NHP and animal research convinced me of its indispensable role in advancing scientific breakthroughs and human health. I view the fellowship as a mechanism to help build and nurture the public's trust in the scientific community – particularly in light of recent notions against science and research from various institutions.

Furthermore, in my role as a clinician, the fellowship enables me to find ways to foster communication and appreciation of the direct impacts of animal research on medicine among patient populations, increasing awareness of biomedical research and garnering public support, which is integral to the long-term outlook of animal-based scientific inquiry.

Q: What do you consider a major breakthrough with primate research and mental health?

A: One of the most exciting recent developments in mental health is the use of brain stimulation to treat psychiatric illnesses. Deep brain stimulation, originally developed for conditions like Parkinson's disease and tremors, is studied and administered to patients suffering from severe depression and other disorders that are resistant to other forms of treatment. Noninvasive stimulation therapies, like transcranial magnetic stimulation, are also incredibly promising, demonstrating the capacity to quickly and significantly reduce distressing symptoms across several disorders in both adults and adolescents.

Both tools target specific parts of the brain involved in emotional regulation and mood to confer therapeutic benefit, and much of the foundational, basic science work elucidating how electrical stimulation influences neurons and broader brain dynamics was conducted in nonhuman primates. The intricate preclinical research examining these technologies in NHPs was and continues to be critical to the success of these life-changing therapies in patients.

Q: How can we better inform the public about research breakthroughs and the value of biomedical research?

A: I think, as scientists, we sometimes have a difficult time with making our research accessible for the public. Science communication isn't emphasized during graduate training, and there aren't built in mechanisms to help students practice translating scientific jargon into layman's terms. Consequently, besides systemic changes in graduate education, I think we have to adopt the stance that broad, accurate dissemination of our findings to the public is a core responsibility of scientists. Another important strategy to consider is investing more resources in primary education to instill lifelong scientific curiosity and appreciation for research and scientific inquiry.

In fact, the national research enterprise depends on the public's support and their trust that investing taxpayer dollars in biomedical research will promote the public good. Practically, this might translate into small steps, including publishing digestible, simple language synopses alongside research articles; updating clinician circles of new findings via mechanisms like grand rounds; and making efforts to feature your research in public-facing university outlets and other local media.

A goal of mine is to connect research awareness groups with patient advocacy organizations, as a means to highlight how scientific discoveries can transform individual patient lives. Patient advocacy groups are deeply dedicated to outreach. Ultimately, human experiences can bring scientific stories to life in a way that data alone cannot and, in turn, spur grassroots support and change.

Q: Finishing your studies and moving into a residency, where do you envision yourself and your research in the next five years?

A: Clinically, I am interested in pursuing child and adolescent psychiatry. I aim to combine my clinical focus with complementary, translational research into a career in academic psychiatry. More specifically, I am interested in the neurobiological mechanisms of early-life psychopathology and the role of brain plasticity in individual differences in susceptibility vs resilience. Kids are remarkably adaptive and agile, and their brains can literally change how they're wired in response to the environment and other factors (even into adulthood in some ways). This means some children in tough circumstances, facing adverse environments, can weather a lot – their brains can change flexibly to respond to their experiences, and they can do very well, we would call this resilience. Other kids, in those same circumstances, might have more trouble adapting, have increased difficulty functioning, and perhaps begin to develop emotional or mental distress. In other words, they may be more susceptible to stress.

What's really exciting is that we're beginning to understand what properties of the brain – on a molecular level – might reflect the adaptive processes we see in behavior. Moreover, there might be ways to enhance or increase these properties – like neuroplasticity or how strong certain connections are in the brain – to change the trajectories of kids who might be more susceptible early in their development to paths of resilience and better mental and emotional health. With that in mind, my goal over the next few years is to start to better understand how longitudinal trajectories of childhood brain development relate to the course of later neuropsychiatric illness. Ultimately, I want to leverage that understanding of neural circuit development and neuroplasticity to work towards novel diagnostic and early-life therapeutic strategies for children and adolescents afflicted by psychiatric disorders.

Q: What recommendations do you have for students who want to begin their journey in primate research?

A: First off, if any part of you, however small, is curious about science and research, get involved in a lab on campus! UW is filled with world-class laboratories and faculty who are enthusiastic about mentoring undergraduate researchers. You don't need to have a specific topic or method you're interested in at this point. Rather, getting exposure to what a career in science looks like is what's most important.

With regard to primate research at UW, labs are collaborative and cross-disciplinary, and many STEM-related projects have connections to animal research. If you're specifically interested in gaining direct experience with primate research, there isn't a place better than UW—Madison to do it. UW houses the Wisconsin National Primate Research Center (WNPRC), one of only a handful nationwide, and it supports cutting edge research in an array of disciplines, including psychiatry, psychology, infectious disease, and regenerative medicine, to name a few. WNPRC faculty are very approachable; browse their lab websites and if you see a project that intrigues you, reach out to show your interest and inquire about opportunities to join their labs!

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