

SPECIAL REPORT SUBARTICLE

What's the hardest part of an autism researcher's job?

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Scientific research is replete with complications and frustrations, large and small, technical and personal.

This year, we asked autism investigators to tell us about the biggest challenges they face as they tackle tough questions about autism. They described a range of difficulties, from coaxing children into imaging machines to needing to carve out time to think. Here's a sampling.

Tackling technology

My biggest challenge is staying at the leading edge of all the technologies that our studies require.

My lab studies zebrafish larvae bearing mutations in autism-linked genes. We aim to describe the flow of information through the brain at single-cell resolution. We have geneticists engineering the mutations in our fish and optical physicists building our microscopes and sculpting light in three dimensions for optogenetics.

Our imaging specialists capture whole-brain activity at high speed. Bioinformaticians make sense of the vast quantities of imaging data from our experiments, searching for salient signals in the brain and differences between mutants and their wild-type counterparts. So I oversee a lot of different types of research, each with its own expert staff.

My background is in genetics and microscopy, and I have to work hard not to be left behind by the team's physicists and mathematicians.

-- **Ethan Scott**, senior lecturer at the University of Queensland in Australia

Facing reality

The hardest part of my job is dealing with the realities of doing research in public schools and early intervention programs. These places are under extraordinary pressures, and research is the least of their concerns. I need to figure out how to be sensitive to their immediate needs while still conducting research that will let us determine which interventions are most effective in community settings and how to help community practitioners implement them.

-- **David Mandell**, associate professor of psychiatry and pediatrics at the University of Pennsylvania

Thought experiments

One huge challenge for me is having the freedom to think and talk, without the need to 'sell' something or the fear that it will be scooped.

-- **Mayada Elsabbagh**, assistant professor of psychiatry at McGill University in Montreal, Canada

Staying still

One of the hardest aspects of the imaging research that we do is acclimating a child with autism to a magnetic resonance imaging (MRI) machine.

It is difficult to complete an awake MRI scan in any child who is younger than 8 or 9 years old, and children with autism pose additional challenges. We start by exposing children to a replica of the real MRI machine, where they practice keeping their heads and bodies as still as possible.

Keeping your head still is somewhat of a foreign concept to a young child, so saying things like "Stay as still as a statue" helps. But providing direct feedback, such as shutting off a movie they are watching when they move their head, works best. Each child requires a lot of training, preparation and patience, something we often forget when we see brain images in research papers.

-- **Rebecca Jones**, assistant professor of neuroscience in psychiatry at Weill Cornell Medicine in New York

Finding families

The technical challenges of recruiting people for research can be quite difficult. We are often approaching families after their initial evaluations, which is a difficult time for them. As a result, it can be hard to get families to see the value in research when the potential benefit is so distant, and

they are so focused on short-term improvements for their child.

-- **Thomas Frazier**, director of the Center for Autism at the Cleveland Clinic in Ohio

Stable salaries

The hardest part of my job is making sure my research team continues to have a job. Ensuring everyone on the team always has a salary does wear on one.

-- **Raphael Bernier**, associate professor of psychiatry at the University of Washington in Seattle

Tripping over trees

I struggle to find balance in the way I portray my role to members of my lab. On the one hand, I want to prepare them for their career choices by being honest and realistic about the frustrations and challenges of being a principal investigator. On the other, I want to share my excitement, joy and sense of fulfillment.

I see lots of students disillusioned with science or pessimistic about academic careers from a very early stage, despite successful role models, and I wonder whether in tripping over the daily 'trees,' we forget to show them the forest.

-- **Lauren A. Weiss**, associate professor of psychiatry at the University of California, San Francisco

Paper pushing

The administrative burdens associated with grants, progress reporting and expenditures can be far more challenging than writing and producing the science.

-- **Michael Talkowski**, assistant professor of neurology at Harvard University

Action items

The biggest frustration is the prevalent conceptualization that behavioral science is a soft science. People think it is so easy to do behavior, yet when their results are not replicable or something goes wrong, they simply conclude that behavioral science is BS.

Behavioral science is trivialized because of its seeming simplicity. The truth is, behavioral science is difficult. Working with animal models of complex human diseases requires training in human psychology, psychiatry, animal behavior, evolutionary biology, genetics, neuroscience and more. What's the use of fancy genetic and molecular technology if we continue to ignore behavioral

experiments, the outcomes of which are used to explain the roles of genetic and molecular factors?

-- **Mu Yang**, assistant professor of psychiatry and behavioral sciences at the University of California, Davis

Picking Projects

We've seen dramatic progress in the genetics of autism, but this has yet to make a difference for most individuals with autism. The difficult choice is knowing which research methods will allow us to move from a list of genes to an effective treatment the quickest.

-- **Stephan Sanders**, assistant professor of psychiatry at the University of California, San Francisco

Thinking big

We're trying to understand how the brain works, and what happens when it doesn't work correctly. It's an immensely complex problem. One of the biggest challenges is to be able to see all the gritty details of each of the lab's projects in progress, and simultaneously see the broad perspective that links the projects into a larger whole. It's easy to lose sight of the bigger picture.

-- **Jessica Cardin**, assistant professor of neuroscience at Yale University