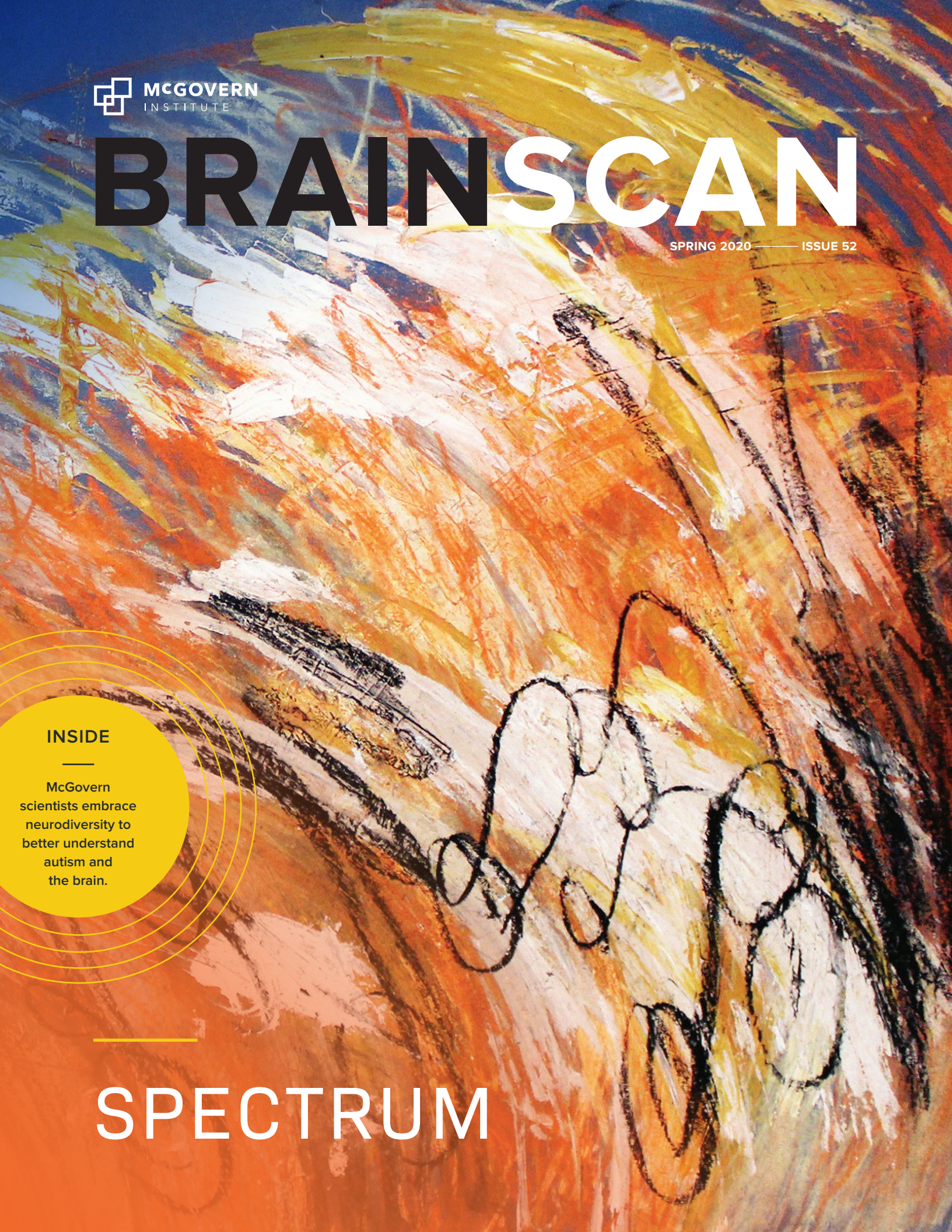


McGOVERN INSTITUTE

BRAINSCAN

SPRING 2020 — ISSUE 52

INSIDE

McGovern scientists embrace neurodiversity to better understand autism and the brain.

SPECTRUM

SPECTRUM

Autism: A mother's perspective

Two of my children are autistic. One presents with more profound symptoms, and the other is on the higher functioning end of the "spectrum."

As such, I have focused on supporting basic research to identify the causes, and most importantly, how to develop therapeutic solutions to ameliorate the most severe symptoms of autism.

I am also determined to help move the needle in enabling true equality and opportunity in the workplace through neurodiversity initiatives. As kids age out of the school system, they deserve to achieve quality of life, happiness, security, and meaningful friendships.

K. LISA YANG

Co-Founder, Hock E. Tan and K. Lisa Yang Center for Autism Research

ON THE COVER

Lisa Yang's son, Doug Tan, is an artist on the autism spectrum who has a particular interest in Herbie, the fictional Volkswagen Beetle. Nearly all of Tan's works include a visual reference (above) to the beloved car.

FOLLOWING AFFINITIES

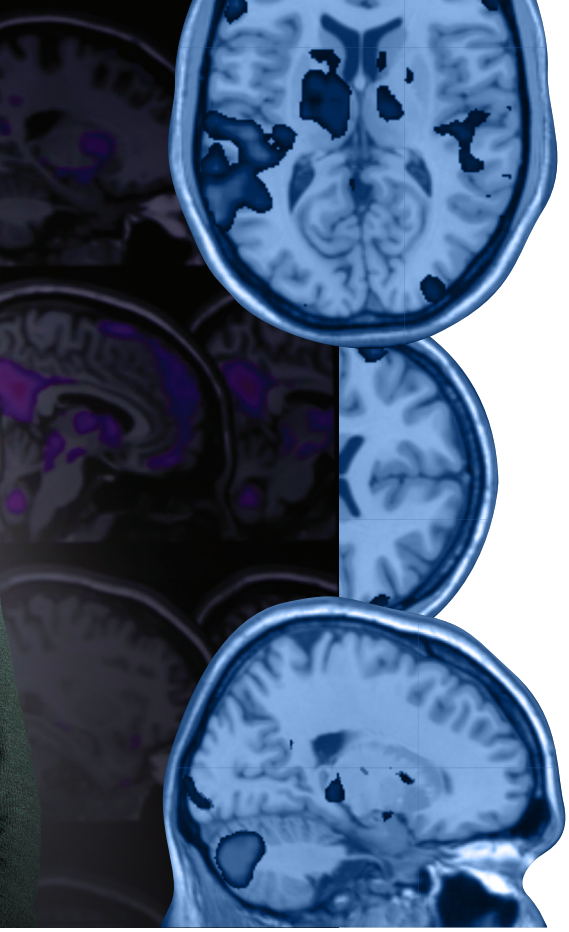
Using personalized, naturalistic experiments, the Gabrieli lab is pioneering new approaches to neurodevelopmental differences.

Researchers often approach autism spectrum disorder (ASD) through the lens of what might "break down." While this approach has value, autism is an extremely heterogeneous condition, and diagnosed individuals have a broad range of abilities.

The Gabrieli lab is embracing this diversity and leveraging the strengths of diagnosed individuals by researching their specific "affinities." Affinities involve a strong passion for specific topics, ranging from insects to video game characters, and can include impressive feats of knowledge and focus. The biological basis of these affinities and associated abilities remains unclear, which is intriguing to John Gabrieli and his lab.

"A striking aspect of autism is the great variation from individual to individual," explains McGovern Investigator John Gabrieli. "Understanding what motivates an individual child may inform how to best help that child reach his or her communicative potential."

Affinities have traditionally been seen as a distraction "interfering" with conventional teaching and learning. This mindset was upended by the 2014 book *Life Animated* by Ron Suskind, whose autistic son Owen seemingly lost his ability to speak around age three. Despite this setback, Owen maintained a deep affinity for Disney movies and characters. Rather than extinguishing this passion, the Suskinds embraced it as a path to



Gabrieli lab members Halie Olson (left) and Anila D'Mello (right) with Kristy Johnson (center) of the MIT Media Lab.

connection. Reframing such affinities as a strength not a frustration, and a path to communication rather than a roadblock, caught the attention of Kristy Johnson, a PhD student at the MIT Media Lab, who also has a non-verbal child with autism.

"My interest is in empowering and understanding populations that have traditionally been hard to study, including those with non-verbal and minimally verbal autism," explains Johnson. "One way to do that is through affinities."

But even identifying affinities is difficult. An interest in "trains" might mean 18th-century smokestacks to one child, and the purple line of the MBTA commuter rail to another. Serendipitously, she mentioned her interest to Gabrieli one day. He slammed his hands on the table, jumped up, and ran to find lab members Anila D'Mello and Halie Olson, who were gearing up to pursue the neural basis of affinities in autism. A collaboration was born.

SCIENTIFIC CHALLENGE

What followed was six months of intense discussion. How can an affinity be accurately defined? How can individually tailored experiments be adequately controlled? What makes a robust comparison group? How can task-related performance differences between individuals with autism be accounted for?

The handful of studies that had used fMRI neuroimaging to examine affinities in autism had focused on the brain's reward circuitry. D'Mello and Olson wanted to examine the language network of the brain—a well-defined network of brain regions whose activation can be measured by fMRI. Affinities trigger communication in some individuals with autism (Suskind's family were using Disney characters to engage and communicate, not simply as a reward). Was the language network being engaged by affinities? Could these results point to a way of tailoring learning for all types of development?

"The language network involves lots of regions across the brain, including temporal, parietal, frontal, and subcortical areas, which play specific roles in different aspects of language processing" explains Olson. "We were interested in a task that used affinities to tap the language network."

By studying this network, the team is testing whether affinities can elicit "typical" activation in regions of the brain that are sometimes assumed to not be engaged in autism. The approach may help develop better paradigms for studying other tasks with individuals with autism. Regardless of whether there are differences between the group diagnosed with

STORY CONTINUES ON PAGE 6

Individuals with autism spectrum disorders report difficulty extracting information from dynamic social cues. McGovern Associate Investigator Rebecca Saxe and research scientist Todd Thompson have been aggregating data on the social brain (such as Theory of Mind regions), from hundreds of participants to estimate how much, and how reliably, changes in social brain regions of adults diagnosed with autism might account for this. The effects of autism are small, and highly variable across individuals.

Going forward this provides important information on robust experimental design to test other hypotheses.

ZOOMING IN ON THE SYNAPSE

A hub for autism risk factors

The human brain contains trillions of synapses—the connections between neurons that allow information to pass from one cell to the next. Within these synapses are hundreds of different proteins, and disruptions of these proteins have been associated with some forms of autism.

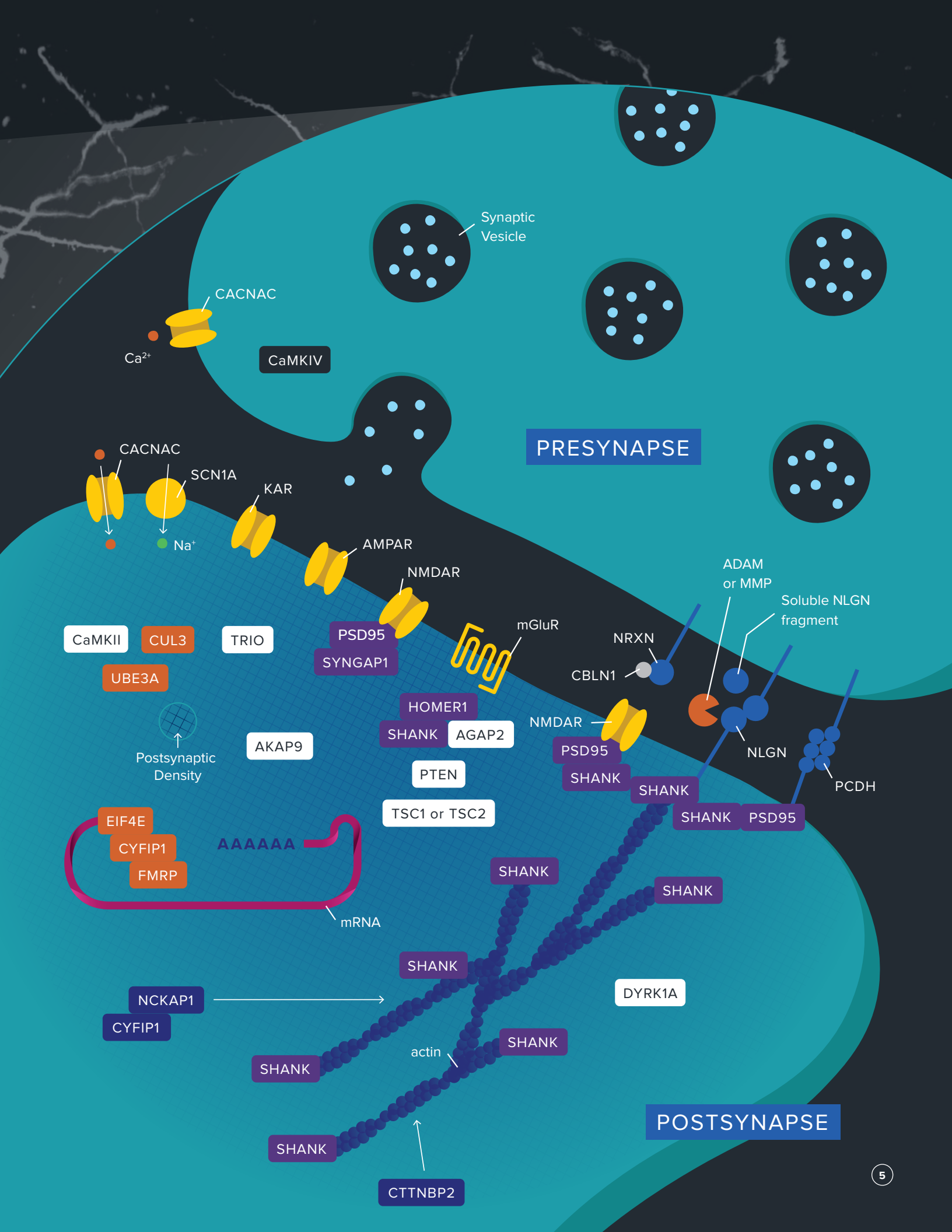
McGovern scientists led by Guoping Feng are untangling the connection between genes that encode for proteins at the synapse and characteristics associated with this brain disorder.

This simplified illustration highlights a few of the synaptic proteins our researchers are studying.

TYPES OF SYNAPTIC PROTEINS

- **CHANNELS AND RECEPTORS**
  allow ions and signals to cross the cell membrane
- **CELL ADHESION MOLECULES**
  connect different cells together
- **SCAFFOLDING MOLECULES**
  provide structural framework for other components of the synapse to be assembled
- **ACTIN MODIFIERS**
  alter the state of the cytoskeleton, a structural component within all cells
- **PROTEIN BALANCERS**
  target protein synthesis and degradation within cells
- **SIGNALING MOLECULES**
  transmit information within cells

Image: Lou Beaulieu-Laroche, Mark Harnett


Synaptic Vesicle
CACNAC
Ca2+
CaMKIV
PRESYNAPSE
CACNAC
SCN1A
KAR
Na+
AMPAR
NMDAR
ADAM or MMP
Soluble NLGN fragment
CaMKII
CUL3
TRIO
PSD95
SYNGAP1
mGluR
NRXN
CBLN1
UBE3A
HOMER1
SHANK
AGAP2
NMDAR
PSD95
SHANK
NLGN
PCDH
Postsynaptic Density
AKAP9
PTEN
TSC1 or TSC2
SHANK
SHANK
PSD95
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NCKAP1
CYFIP1
DYRK1A
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actin
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POSTSYNAPSE
SHANK
CTTNBP2

CONTINUATION OF STORY FROM PAGE 3

autism and typically developing children, insight will likely be gained into how personalized special interests influence engagement of the language network.

The resulting study is task-free, removing the variable of differing motor or cognitive skill sets. Kids watch videos of their individual affinity in the fMRI scanner, and then listen to stories based on that affinity. They also watch and listen to "neutral" videos and stories about nature that are consistent across all children. Identifying affinities robustly so that the right stimulus can be presented is critical. Rather than an interest in bugs, affinities are often very specific (bugs that eat other bugs). But identifying and cross-checking affinities is something the group is becoming adept at. The results are emerging, but the effects that the team are seeing are significant, and preliminary data suggest that affinities engage networks beyond reward circuits.

"We have a small sample right now, but across the sample, there seems to be a difference in activation in the brain's language network when listening to affinity stories compared to neutral stories," explains D'Mello. "The biggest surprise is that the differences are evident in single subjects."

FUTURE FORWARD

The work is already raising exciting new questions. Are there other brain regions engaged by affinities? How would such information inform education and intervention paradigms? In addition, the team is showing it's possible to derive information from individualized, naturalistic experimental paradigms, a message for brain imaging and behavioral studies in general. The researchers also hope the results inspire parents, teachers, and psychologists to perceive and engage with an individual's affinities in new ways.

"This could really help teach us to communicate with and motivate very young and non-verbal kids on the spectrum in a way that is interesting and meaningful to them," D'Mello explains.

By studying the strengths of individuals with autism, these researchers are showing that, through embracing neurodiversity, we can enhance science, our understanding of the brain, and perhaps even our understanding of ourselves.

Interested in learning more about autism studies at MIT?

Visit autismresearch.mit.edu or email autism@mit.edu

"Aggression is one particularly disruptive symptom in severe forms of autism. We're taking a genetic approach to examine the brain circuitry linked to aggression in mouse models of ASD."

—ALEXANDRA KROL, J. DOUGLAS TAN POSTDOCTORAL FELLOW, HOCK E. TAN AND K. LISA YANG CENTER FOR AUTISM RESEARCH

COMPUTATIONAL NEUROSCIENCE

Neural Networks

A new computational model from the **DiCarlo** lab has re-imposed a brain-like architecture on an object recognition network. The result is a shallow-network architecture with surprisingly high performance, indicating that we can simplify deeper networks yet retain high performance in artificial learning systems.

CELLULAR & MOLECULAR NEUROSCIENCE

Neuron Navigation

The organization of many neurons wired together in a complex circuit gives the brain its ability to perform powerful calculations. Work from the **Harnett** lab recently showed that even single neurons can process more information than previously thought, representing distinct variables at subcellular regions, called soma and dendrites, during behavior.

Addictive Behaviors

Repetitive movements such as nail-biting are often seen in humans under the influence of habit-forming drugs. Studies in the **Graybiel** lab have found that these repetitive behaviors may be due to a breakdown in communication between neurons in the striatum—a deep brain region linked to habit and movement.

COGNITIVE NEUROSCIENCE

Controlling Attention

The **Desimone** lab has found that people can enhance their attention by controlling their own alpha brain waves based on neurofeedback they receive as they perform a particular task. This is the first time that this cause-and-effect relationship has been seen, and it suggests that it may be possible for people to learn to improve their attention through neurofeedback.

Brain Biomarkers

Finding new methods for discovering early biomarkers for risk of psychiatric disorders would allow early interventions and avoid reaching points of crisis. **Susan Whitfield-Gabrieli** and colleagues found that signatures predicting future development of depression and attentional symptoms can be detected in children as young as seven years old.

Awards

NANCY KANWISHER | 2019 George A. Miller Prize in Cognitive Neuroscience

SAM RODRIQUES (BOYDEN LAB) AND JONATHAN STRECKER (ZHANG LAB)
2019 STAT Wunderkinds

In Memoriam

We regret to note that Donald C. Berkey ’42 SM ’43 passed away in late 2019. Together with his wife Doris, Don established an endowed professorship in neuroscience currently held by McGovern Institute director Robert Desimone. The Berkeys were passionate about furthering novel research into complex brain disorders such as mental illness and Alzheimer’s.

DID YOU KNOW

88%

of children on the autism spectrum have an affinity — or special interest that they are particularly passionate about?

We are curious about this.

The Gabrieli lab is exploring the brain basis of these special interests in kids with and without autism. The PAL (Project on Affinities and Language) study uses noninvasive and child-friendly fMRI methods to study whether affinities can activate language regions of the brain.

The lab is currently looking for 7–12-year-old children with and without autism who have a special interest or passion.

Interested in participating? Sign up at:
bit.ly/PALkids or email autism@mit.edu

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