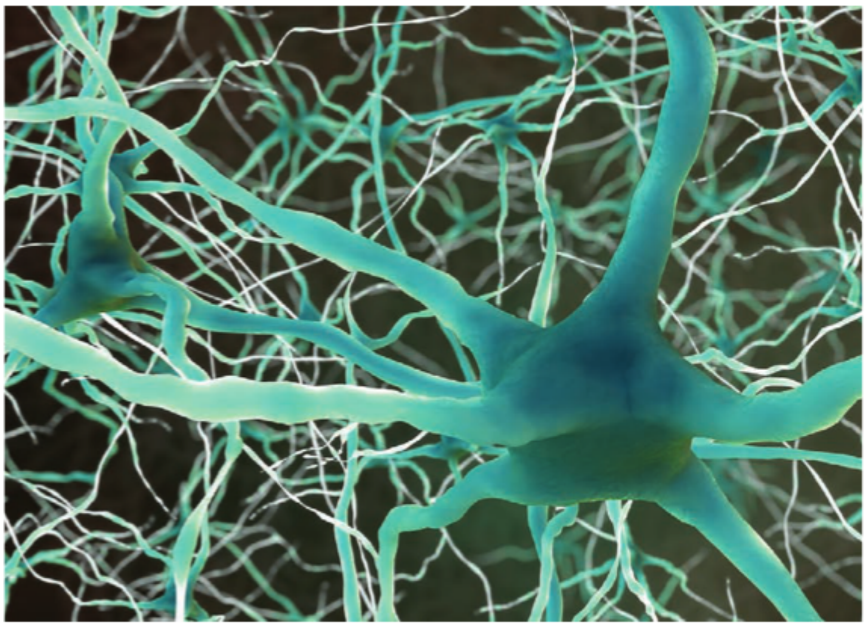
RESEARCH

The Brain's Sensory Switchboard

A scientist maps the neural circuits that allow us to pay attention, and opens new channels for treating mental disorders.



Times Square in New York City bombards the senses with bright lights, blaring sirens, funky smells, and jostling crowds. But amid the chaos, your brain manages to filter out distractions and focus on the task at hand, be it finding a restaurant or getting to the theater. "From moment to moment we typically use a very small percentage of incoming sensory stimuli to guide our behavior," says neuroscientist Michael M. Halassa, MD, PhD, assistant professor of neuroscience and psychiatry at NYU Langone and its Druckenmiller Neuroscience Institute. "That's why the McDonald's sign pops up when you're hungry and marquees suddenly appear when you're looking for Broadway shows."

How does the brain selectively filter a nonstop barrage of sensory information? The question has implications far beyond getting a burger before a matinee. "In many neurological disorders the brain is overloaded," says Dr. Halassa, whose research on the topic has earned him a prestigious 2015 Sloan Research Fellowship. "In schizophrenia, autism, and ADHD, it may be that the brain is unable to properly control sensory input because this filtering function is broken."

The answer, according to recent findings from Dr. Halassa and his team, may lie in a shell-shaped region in the center of the mammalian brain, known as the thalamic reticular nucleus, or TRN. This tiny part of the brain consists of a thin layer of cells on the surface of the thalamus, a region that relays sensory information from the body to different destinations in the cortex, the "gray matter," or thinking part of the brain.

Since Dr. Halassa joined NYU Langone in 2014, his experiments with mice have revealed — in unprecedented detail — how the TRN acts as a switchboard to filter incoming sensory stimuli and focus attention. In one study, he and his colleagues looked at differences in TRN activity between sleeping and awake mice. By recording the activity of individual cells, they found that TRN cells blocked the flow of sensory information during sleep and opened the gates when the mice were awake. Then, by switching on or off individual TRN cells, the scientists were able to induce sleepy or alert behavior in the mice (see "The Big Idea: What's at the Root of Consciousness?" on the facing page).

Dr. Halassa's team also discovered that individual TRN cells are tuned to specific senses — some modulating vision, others hearing, and so on. In research published in *Nature* last year, they showed how these cells augment some sensory signals and dampen others, so that mice focused on finding a food reward and blocked out distractions.

"There is a huge effort that the brain puts into inhibiting irrelevant inputs. Without a reticular nucleus we'd be utterly distracted."

MICHAEL HALASSA, MD, PhD

This study could be game-changing for the scientific understanding of attention. To date, most research has put the cortex center stage, in the belief that it selects which information to focus on. Dr. Halassa's team discovered that, instead of filtering information directly, neurons in the cortex may tune the brain to sights and sounds by sending signals to "inhibitory" TRN cells that block information.

"The change in sensitivity to incoming sensory stimuli is occurring at the level of the thalamus, and it occurs by the prefrontal cortex telling the TRN which senses to augment and which senses to suppress," Dr. Halassa explains.

The results set the stage for studying exactly how much "distracting" information the TRN can block or permit, and how this mechanism can malfunction in animal models of disease, such as autism. "Now we have a circuit that we know is involved in turning the volume up and down on incoming sensory stimuli, and we can study it," says Dr. Halassa. "We can investigate whether individuals with autism have a broken reticular nucleus, and ultimately, develop drugs that can rescue some of the sensory deficits and sensory overload in autism." ■

THE BIG IDEA

What's at the Root of Consciousness?

As a medical student in his native country of Jordan during the 1990s, Mike Halassa, MD, PhD, became fascinated by the long-standing mystery of where consciousness lives in the brain. It was a question that had also perplexed his hero, Nobel Laureate Francis Crick, the British biologist who helped decode the double helix structure of DNA.

Like Dr. Crick, Dr. Halassa's interest in how matter becomes imagination quickly led him to a thin *C*-shaped structure in the brain sandwiched between the thalamus and the cortex, called the thalamic reticular nucleus, or TRN. Once thought to be a simple extension cord between the center of the brain and its exterior, the TRN is now emerging as a sophisticated switchboard for sensory information, thanks in large part to Dr. Halassa's innovative research.

Over the past few years, his team has created the most extensive map of the TRN to date, revealing a complex network of cells that tune the brain to different sensory information, turning the volume up or down depending on the task at hand. While the question of consciousness as a biological phenomenon remains an intellectual challenge, Dr. Halassa has discovered a provocative clue in the TRN, showing that it helps us block out sensory information while we sleep and lets it in while we're awake. More important, he has revealed an entirely new neural circuit underpinning attention, which has far-reaching implications for the treatment of sensory disorders like schizophrenia, attention-deficit disorder, and autism.

"There is a huge effort that the brain puts into blocking irrelevant inputs," Dr. Halassa says. "Without a reticular nucleus we'd be utterly distracted."

RESEARCH

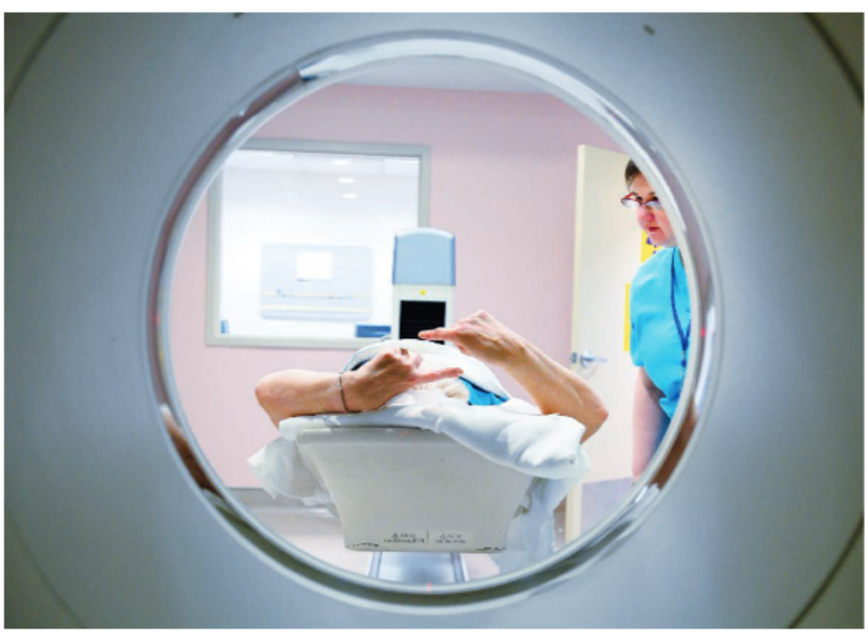
A Radiology Rethink

NYU Langone researchers launch a laboratory to overhaul how radiology works in complex healthcare systems nationwide.

"Radiology is a canary in the coal mine for all kinds of things in healthcare systems," says Leora Horwitz, MD, associate professor of population health and medicine at NYU Langone. All too often the communication between the radiologist and non-radiologists is fragmented and incomplete. Take a routine X-ray. There could be multiple specialists ordering, performing, interpreting, and following up on the exam, and opportunities for mishaps mount with each transition. Multiply that by 400 million — the number of radiology tests performed in the United States each year — and the result is a $100 billion industry strained by over-testing and medical errors.

Last October, Dr. Horwitz, in collaboration with colleagues in the departments of population health and radiology, received a $4 million grant from the U.S. Agency for Healthcare Research and Quality to comprehensively redesign the Medical Center's radiology systems. With the new grant, the researchers are creating a laboratory — the NYU Langone Patient Imaging Quality and Safety Laboratory (PIQSL) — to apply a design and engineering approach to transforming the practice of radiology. One of 13 patient-safety learning laboratories across the country, PIQSL is bringing together clinicians from an array of NYU Langone medical departments, along with operations researchers, experts in public policy and business, and organizational-systems designers.

The team will analyze in fine detail the current processes of ordering ambulatory radiological tests and inpatient interventions, and coordinating the follow-up to imaging studies. To fully understand the complexities of radiological testing in different healthcare environments, they will then prototype and test new systems — and revise and test these systems again and again — to evaluate their efficacy at NYU Langone. Finally, they will compare the Medical Center to other institutions.



400 M

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Dr. Leora Horwitz co-leads the PIQSL team with Drs. Danny Kim, Eric Aaltonen, and Soterios Gyftopoulos, all assistant professors in the department of radiology, along with Dr. Scott Braithwaite, professor in the department of population health, and Dr. Danil Makarov, assistant professor in the departments of population health and urology.

"The laboratory is a true collaboration between population health and radiology," says co-project leader Danny Kim, MD, assistant professor of radiology. "It's all about figuring out how radiologists and non-radiologists can work together more effectively."

Ultimately, in four years, the team aims to produce a national strategy to improve the safety and value of radiological testing.

For Dr. Horwitz, the PIQSL project is one among several that attempts to bridge gaps in care. As founding director of NYU Langone's Center for Healthcare Innovation and Delivery Science (CHIDS), she also leads the Greater New York York City Practice Transformation Network, one of 29 such networks across the country selected last year to participate in a $7-million federal grant to help doctors improve the quality of outpatient care while reducing costs.

The Network includes some 2,000 clinicians from the NYU Langone Faculty Group Practice, NYU Lutheran, and other partners. "It's incredibly diverse in terms of doctors, patients, and practice environments," says Dr. Horwitz. "NYU Langone is the perfect place for this research because the medical school and the hospital are so integrated, and NYU Langone is an institution that really cares about quality." ■

THE BIG IDEA

Changing the System

"Healthcare seems not to work as well as it should," says Leora Horwitz, MD. Dr. Horwitz understands the problems both as a clinician — a hospitalist at NYU Langone since 2014, and a primary care doctor before that — and as a researcher.

As director of CHIDS, Dr. Horwitz's strategy for optimizing healthcare is to understand all the working parts involved in the total care of a patient, from the check-in, the exam, the follow-up, and all the behind-the-scenes steps in between. Then it's possible to tinker with these working parts and devise new and better systems.

"The healthcare system is my laboratory," she says.

Recently Dr. Horwitz and colleagues have been looking closely at one very specific medical transition — the discharge of patients at NYU Langone who have had major heart, joint, or spine surgery. "As clinicians, we often feel that discharging patients to an acute rehabilitation facility may help them recover better and prevent them from returning to the hospital," Dr. Horwitz says.

But their new study, recently published in *JAMA Internal Medicine*, found that sending more patients home for post-surgery recovery did not affect the rate of hospital readmission after surgery. Says Dr. Horwitz, "These results may give surgeons greater confidence in discharging patients directly home instead of to a facility, where care is more costly and potentially more disruptive to the lives of patients and families."