by **Carolyn Shapiro** | photographs by **Andy Duback**

RESEARCH THAT RESONATES

UVM's MRI Center for Biomedical Imaging opens a window into brain function for many researchers.

Inside the giant tube of the magnetic resonance imager at UVM's MRI Center for Biomedical Imaging, a woman who is one of the study subjects of Julie Dumas, Ph.D., lies prone as she performs a memory test.

Letters flash on a computer screen above the subject's head, and she presses a button when they match in a specific order. Wedged between bolsters, the woman wears headphones and a helmet shaped like something a Star Wars stormtrooper would wear, which records images from her brain.

"This is a measure of working memory," Dumas, an associate professor of psychiatry, explains over the loud whirring and banging of the MRI in the adjacent room. "It's the ability to keep a small amount of memory in mind over a short period of time and to use that information. We can see how much of your brain is used during this memory test."

Dumas specializes in research related to cognition and aging and conducts much of it in the MRI Center, the College of Medicine's research facility housed at the UVM Medical Center. Her current study explores the factors that cause women to experience menopause differently and involves 115 subjects between age 50 and 60.

"We're interested in how a particular gene affects the brain in women after menopause," Dumas says.

The MRI shows Dumas the areas of the brain that activate during the memory test. The machine detects blood flow, which indicates the electrical and chemical signals taking place where the brain is working.

"All of my research is about brain functioning," Dumas says. "We don't want to just know how menopause affects your memory. We want to know how your brain functions."

The MRI, she says, is crucial to her and her fellow neuroscientists' work. Their research on Alzheimer's disease, attention deficit hyperactivity disorder, adolescents, and addiction all has involved heavy use of the machine.

"It's amazingly cool technology," says Hugh Garavan, Ph.D., a UVM professor of psychiatry who studies brain function particularly in children and teens. "What this enables us to do is to see the brain in action in a living, breathing person."

The MRI can capture most psychological, intellectual and emotional responses, Garavan says. When someone does a math equation, one area of the brain "lights up" to indicate activity. If that person thinks about a funny movie scene, another area lights up.

"This is the most complicated thing in the universe," Garavan says, pointing to his temple. "And we still haven't mapped it all out."

The MRI Center was pivotal in securing the College of Medicine's role in a National Institutes of Health grant for a landmark, long-term study of about 10,000 children and their brain development, starting at age 9 or 10. All 19 sites participating in the project had to have a top-notch MRI capable of crunching lots of data at high speeds. The researchers — led by Garavan and including Dumas and others at UVM — will look at the children's brain markers for resilience, creativity, academic performance, risk of drug and alcohol use and mental, emotional, and behavioral problems.

"You have to have a lot of flexibility to tweak the machine," Garavan says of the MRI. "It's just a more high-tech piece of kit. So these studies couldn't happen without that research-dedicated machine."

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In 2007, with the help of federal funding, UVM installed the Achieva 3T, made by Dutch company Royal Philips. (The "T" in its name stands for "tesla," the unit of measurement for a magnetic field.) It is essentially the same in construction as other MRIs used in the hospital to take detailed images of anatomical structure and soft tissue.

An MRI scanner uses a powerful magnet and radio waves to excite water molecules in the body. A nest of electric coils alter the magnetic field to target different areas of anatomy. Radio waves are sent to the molecules, which respond with their own signals. Radio receivers capture those signals, and the MRI creates images from the magnetic properties of the tissue.

The MRI releases no radiation, so research subjects can spend as much time in the tube as necessary without risk, unlike a CT (computerized tomography) scan.

"It is still the most impressive piece of engineering that I can think of," says Assistant Professor of Radiology Joshua Nickerson, M.D., co-director of the MRI Center for Biomedical Imaging.

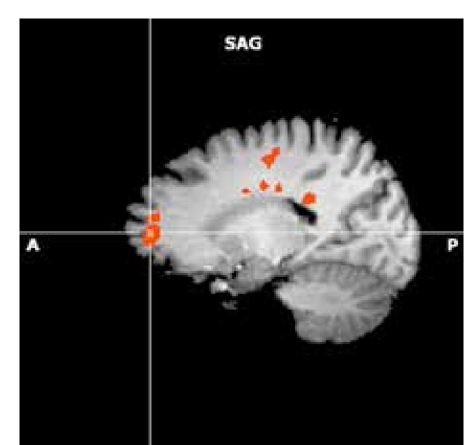
Much of the research done with the scanner is known as "functional" MRI, because it looks at brain function. The machine also does diffusion imaging, which can highlight "white matter," the connections between various areas of the brain — showing how the brain is wired.

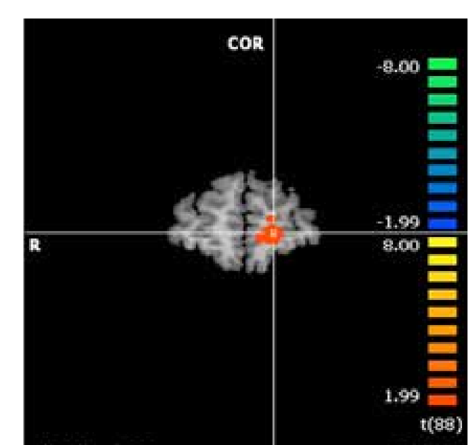
What makes the research MRI unique isn't the technology itself but the way it is used. It is coaxed, tweaked and prodded — with the help of software coding and computer science — into different "sequences" for collecting and analyzing the data it generates.

"We have amazing flexibility with this machine," says Associate Professor of Radiology Richard Watts, Ph.D., who co-directs the MRI Center with Nickerson. "It's not like a CT scan, where you just get a single image."

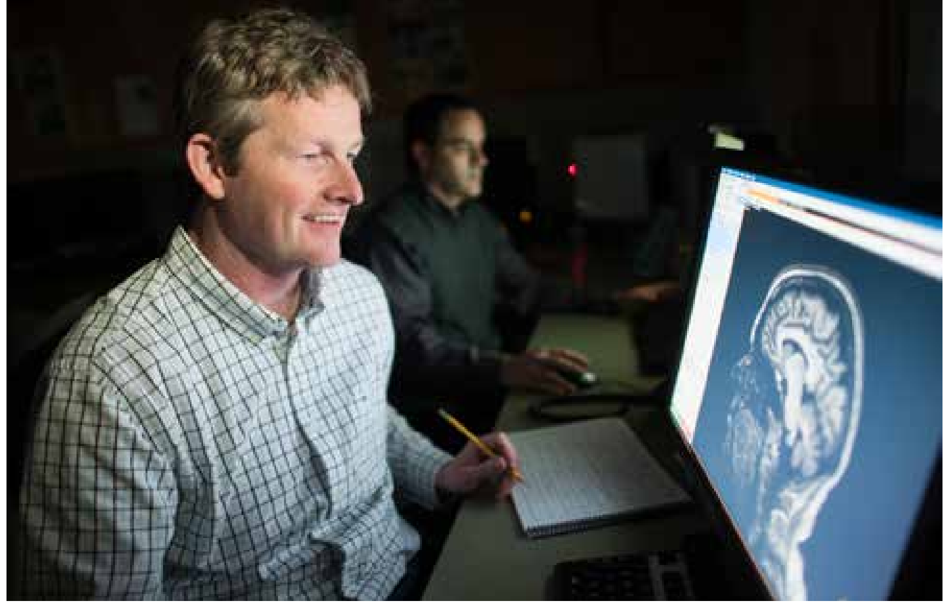
For MRI imaging, the brain is separated into tens of thousands of tiny regions, each with millions of neurons and tens of millions of connections between

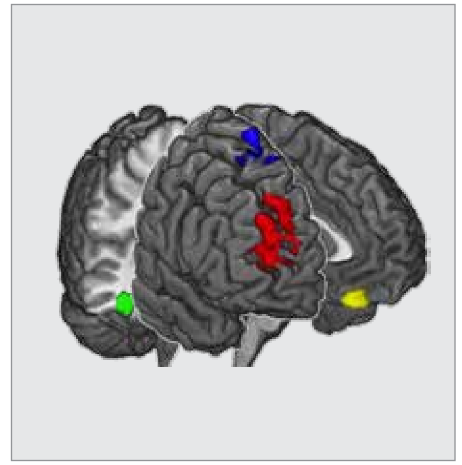
Jay Gonyea, administrator of the MRI Center for Biomedical Imaging, and Associate Professor of Psychiatry Julie Dumas, Ph.D., prepare a research subject in front of the circular magnet of the MRI.





MRI images that Julie Dumas, Ph.D., used for a study on memory in older adults show activity in the front of the brain, where memory function usually takes place when people age. Activity in the brain is indicated by red coloration, which shows increased blood flow where the brain is working. Dumas gave her study subjects a substance that shifted brain activation from front to back, mimicking the way the brain would function in a younger person. Without the MRI, Dumas says, she would have no way to see the change in brain function.





In brain images taken by the research MRI at the University of Vermont, Hugh Garavan, Ph.D., UVM associate professor of psychiatry, found that teens who were most resilient and able to bounce back when faced with adversity — such as a death in the family or a parents' divorce — had a higher volume of grey matter in their frontal lobes, as indicated by the red and blue colored areas. The brain's frontal lobe is involved in self-regulation, control of emotions and management of stress. Resilience was one of many factors that Garavan found can help predict whether an adolescent will become a binge drinker.

those neurons, Garavan says. For his NIH study, the MRI recorded brain activity in every region every two seconds while his subjects performed a task. Watts is trying to boost that recording speed to less than one second, Garavan says. "That will help us better localize where those signals come from," Garavan says. "And the nice thing about it is you get to see what's going on in the whole brain."

Nickerson describes the research MRI work in logging terms. It can cut down trees like any chainsaw. But in the hands of a talented operator or a true visionary, it can also carve beautiful artwork out of a wooden stump. In the same way, it takes a talented scientist to turn the magnetic tool into an agent of artistry.

In the research MRI's case, Watts is the chainsaw artist. He is considered the MRI guru at UVM, the brain power behind brain imaging.

His fellow researchers and MRI staff speak of him with reverence, citing his genius for digging out unique and ground-breaking techniques. Watts adjusts the machine to make it more sensitive to the specific areas that the scientist wants to study.

It can focus on protein in the brain, looking for increases in amyloid or tau, substances that are associated with Alzheimer's disease. It can measure fluid that builds up in tissue surrounding a brain tumor, helping to determine how aggressive the cancer is and treatments that might work best.

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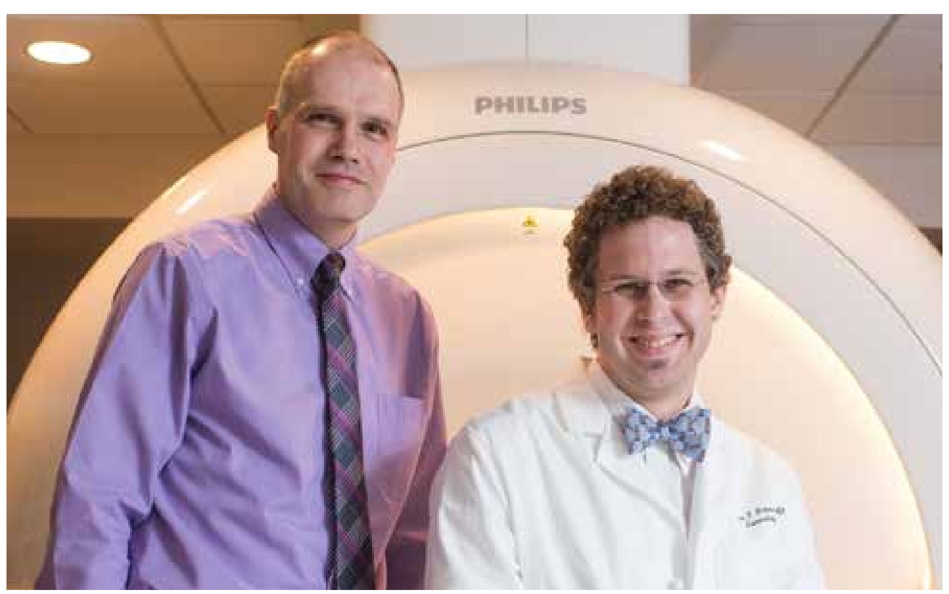
For a study in emergency medicine, Watts has set the MRI to pick up brain temperature for researchers who know that cooling the brain can help after a heart attack and want to understand the cerebral response to temperature changes.

"Those guys push a button and it looks cool," Garavan says of Watts and the MRI technologists who operate the machine, "but there's a whole complicated process to get those pictures."

Watts stays in frequent contact with the Philips company. The relationship with the manufacturer often garners early access to the latest improvements and new features of the technology. At the end of 2013, UVM's MRI was the first in North America to receive its "dStream" upgrade, which took the system from analog to digital, Watts says. That means it doesn't produce as much "noise" or lose as much fidelity as it transfers signals, which improves image resolution.



Professor of Radiology Richard Watts, Ph.D., left, and Professor of Radiology Joshua Nickerson, M.D., are co-directors of the MRI Center for Biomedical Imaging.

"We're known as being a strong technical group," Watts says, "and we're trying to push that technology right to the limit."

UVM is a "luminary" site for Philips, demonstrating the technology for other institutions that are considering the MRI, says Jay Gonyea, M.S., administrative director of the MRI Center. In exchange, the company discounted UVM's price for the equipment, which typically runs about $1 million per tesla, he says.

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Before the research MRI arrived, Dumas had to schedule her study subjects around the availability of the hospital scanners. The timing wasn't always practical. If she had access at 4 p.m., but her subjects needed to fast overnight and take a drug in the morning before a test, they couldn't wait until the afternoon.

The beauty of the research MRI is that, with it, researchers can pursue what-if scenarios and test theories, says Alexandra Potter, Ph.D., assistant professor of psychiatry.

"It helps us answer fundamental questions we couldn't answer any other way," she says.

Potter likes to try out her research regimen in the machine herself to make sure she understands her subjects' full experience. "It makes you a better scientist, for sure," she says.

The MRI has assisted Potter with studies of nicotine in the brain and its ability to temper impulsivity in young people with ADHD. Now, she is working with Watts to develop a better MRI view of the cerebellum, which is located at the back of the brain and controls motor function. It is typically dismissed as an influence on cognitive areas, but Potter has noticed in MRI images that the cerebellum looks different in people with ADHD and is pursuing a new study in that area.

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Assistant Professor of Psychiatry Alexandra Potter, Ph.D., has used the MRI Center for Biomedical Imaging to further her research on the nicotine in the brain and its effects on impulsivity in young people with ADHD.

"Maybe the cerebellum affects cognition, and we just didn't know that," she says.

The MRI Center currently is involved in about 40 projects and welcomes any scientists who can take advantage of the technology, Gonyea says. Researcher Bruce Beynnon, Ph.D., professor of orthopaedics, has used the MRI to study knee joints. The MRI has scanned mice to show Naomi Fukagawa, M.D., Ph.D., professor emerita of medicine, the development of disease in rodents exposed to biodiesel or petrodiesel *in utero*.

Watts even invented an MRI method to measure tubes of sand that George Pinder, Ph.D., the renowned UVM engineering professor, created to simulate groundwater contamination.

"It gives you a different piece of the puzzle that you're trying to put together," Gonyea says. "It gives you more answers to the questions that you're researching."

It's the insight into the workings of the brain, though, that make the research MRI so fascinating, Nickerson insists. Every brain is unique, like a snowflake. Likewise, every brain responds in a unique way to humor, sadness, education, tragedy, drugs, illness and aging. For researchers like Dumas, the MRI acts as a window to better understand the complexity of this exceptional organ — and the possibility of making it stronger and healthier.

"My goal is to learn more about how we can predict the bad stuff in the future," Dumas says. "Once you're 70 and losing your memory, it's too late. So I want to see what's happening now ... and what we can do about it." VM