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By Their Bootstraps

Brain imaging in the Show-Me State By Nelson Cowan, PhD

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At the recently opened Brain Imaging Center at the University of Missouri-Columbia, researchers have MRI technology at their disposal to study diseases such as Parkinson's, autism, and other neurocognitive disorders. It is quite rare for an academic department to operate such a facility, and, before it existed, members of the Department of Psychological Sciences had to perform research at the university hospital. The center is open to other departments and surrounding industries, and offers an opportunity for researchers from different fields to meet one another.

The Brain Imaging Center at the University of Missouri in Columbia is not housed in the most imposing structure in the world. It is not part of a medical center and cannot receive clinical work; it is dedicated to research. In the Melvin H. Marx Building atop a hill, the building is actually shared with artists creating pottery and firing it up from time to time in large kilns in the backyard.

The two groups, though, have a friendly co-existence and are careful not to interfere with each others' work. They leave doors shut in order to keep any pottery dust from escaping to the scientific wing (and occasionally to protect the privacy of nude models in the artistic wing), but artists and scientists sometimes stop to chat in the parking lot and on occasion even compliment each others' successes at turning ideas into results.

The Brain I maging Facility

Inside the recently built brain-imaging half of the building, one arrives at the receptionist's desk in the warm, earthy green office and may be greeted by Bret Glass, MA, an assistant with considerable knowledge about psychology, the brain, computer technology, and safe neuroimaging procedures. Storing metallic objects and other belongings in large wooden lockers with non-magnetic keys (because metal objects could fly into the scanner), one can proceed with Glass or another trained employee through several locked doors to find a 3-Tesla Siemens Trio MR scanner in a roomy and safe environment. Adjacent to it is a well-designed and even more spacious control room with desk space, computers, portals, and a good view of the scanner.

The building design was based at least in part on what the experienced imaging faculty at Washington University in St. Louis said they wished they had thought of when they built their center, and it is designed to facilitate collaboration with them.

Outside of the high-security zone, there is adjoining space occupied by several important amenities. There is a room with a mock scanner, which looks like a real one and comes equipped with a participant table that moves in and out of the bore. It is used to teach participants to keep still while in the bore, and also to collect behavioral data, using button-press responses feeding into a computer program. This inexpensively provides behavioral results so that the procedure to be used in the actual scanner can be fine-tuned ahead of time.

There are several testing rooms and a sunny conference room that can hold about 20 people, and computers are scattered about. Ongoing construction on the second floor will provide space for behavioral and electrophysiological laboratories, several offices, and data analysis activities. Some of the analysis space is intended to be library-like in its quietude; other space is intended for lively technical discussions.

Pulled up by the Bootstraps

It is quite rare for an academic department to operate a brain imaging center. Before this facility existed, several professors in the Department of Psychological





The fMRI method on Missouri's scanner. Three views of a brain with colored spots indicating fMRI results from finger-tapping, which activates neurons in the contralateral motor cortex and the ipsilateral cerebellum. (Shawn Christ, PhD)



The diffusion tensor image (DTI) method on Missouri's scanner. DTI results in images of neural fiber tracts with different color coding for tracts extending in different directions. (Shawn Christ, PhD)



Steven Hackley, PhD, of the University of Missouri, right, shows an image to Hiroaki Masaki, PhD, a visitor from Waseda University in Tokyo (Nelson Cowan, PhD)

2/25/2009

rt-image.com: By Their Bootstraps: B...

Sciences had to get their brain research done the more usual way: by paying for, and signing up for, time in an MR scanner at the university hospital. One problem with that approach was that research had to take a back seat to clinical needs. It was difficult to find free time on the scanner except during the weekends – especially in the late hours of the weekend nights. Then, it was often difficult to arrange for a technologist to be available at the right time.

Even with those hurdles passed, the session sometimes had to be postponed to let in a clinical case that could arise suddenly, perhaps from an injury or stroke. Without a research contract with the scanner company in place, data were sometimes erased during routine maintenance. In the old days, this occasionally resulted in the loss of data. The researchers were demoralized, and a few were lost to other universities with better MR access.

Then, about four years ago, the department, college, and university got together and pulled themselves up by their bootstraps. Here is how it happened. With pleas from the Cognition and Neuroscience Training Area of the department, a plan was hatched by the department chair at the time, David Geary, PhD. There was support from two consecutive deans of the College of Arts and Science, Richard Schwartz, PhD, and Michael O'Brien, PhD, and from the chancellor of the university, Brady Deaton, PhD.

Funding was secured for a position called the Miller Family Chair in Cognitive Neuroscience. This faculty member has not yet been hired, but, when the hire is made, the individual will have the option of taking over as director of the center. In order to help secure this endowed chair and the imaging center, the department pledged to dedicate to neuroimaging several unfilled professors' lines in cognition and neuroscience.

The next department chair, Ann Bettencourt, PhD, took over where Geary left off, in her words "with the help of many knowledgeable and committed faculty members in the department." With these resources in place, the department pledged to back up the effort fiscally. The urgent need for an MR scanner was clear, and the university provided funds (through a zero-interest, long-term loan) to build the new center and purchase the scanner. In all, the cost came to just less than \$4 million. The business model for the Brain Imaging Center to repay the university involves allowing any researcher with a workable plan, from the university or outside of it, to use the center for a reasonable fee.

At various points, several cognitive psychologists helped. Michael Stadler, PhD, helped Geary write the plan; Jeffrey Rouder, PhD, who has a background in physics, later helped negotiate the purchase of a scanner; Moshe Naveh-Benjamin, PhD, supervised building procedures; and I then took over as director of the center. My main effort now is on acquiring the complement of the necessary expert staff and obtaining more grant funding to support research in the center. Several researchers already have relevant grant funding, and there are grants from the center to allow the collection of pilot data necessary to apply for additional extramural funding.

The Department of Psychological Sciences already has several faculty members with extensive experience collecting MR data. Many other researchers who have expressed an interest in carrying out an MR study have little or no experience with the technique. To get them started, the center is providing help from technologists at a modest cost, with advice from expert faculty as necessary. This help can include both collecting MR data and processing it. It is meant to be a center at which research can be conducted in a convenient, user-friendly, and welcoming manner. So far, it seems to be working well.

The Methods and Studies

When the center opened, expert help was obtained from an MR physicist from Baltimore, Moriel NessAiver, PhD, who was able to check out the scanner in great detail and gave it an excellent bill of health. The faculty using it depend most heavily on several methods: structural MRI (sMRI), functional MRI (fMRI), and diffusion tensor imaging (DTI).

The purpose of sMRI is to get a highly detailed picture of the brain with its anatomical structures visible, as is often performed in a clinical setting. Sometimes, this is of use because there are pathologies involving abnormal brain structures. This method measures the density and consistency of tissue to indicate where brain structures are.

On top of a basic sMRI image, though, most of the psychologists add on colored spots of different shapes and sizes to represent the areas of the brain that are active in certain tasks, using the fMRI method. The fMRI method works by detecting slight changes in the level of oxygen in the blood caused by activity in

lokyo (Nelson Cowan, PhD)



Theresa Becker lifts the head coil to prepare to carry out a scan on fellow graduate student Elizabeth Martin (Nelson Cowan, PhD)



In the conference room, Nelson Cowan, PhD, director of the Brain Imaging Center, explains to Bret Glass a formula for the contents of working memory (Steve Hackley, PhD)

2/25/2009

the brain, measured while research participants carry out different sorts of tasks that can be compared to one another.

The tasks typically involve an image that is projected onto a screen in the scanner while the participant is lying down watching it; on headphones that can convey clean, crisp sounds in the scanner despite the background whines and clicks that the magnetic machinery produces; and on a button-box for responses, which rests on the participant's chest during the scans.

For example, in one task, the participant might be asked to read a word silently; in another task, the participant might be asked to read the word and also memorize it. Each task produces an extensive pattern of activity, but, when the two patterns are compared statistically, excess activity in certain limited areas indicates the regions of the brain especially involved in the memorization process that defines the difference between the two tasks.

Finally, in DTI, the movement of molecules is tracked in order to get a very clear picture of the fiber tracts in the brain.

In the Department of Psychological Sciences, several researchers already have published neuroimaging studies. Shawn Christ, PhD, an assistant professor, uses fMRI and DTI with various tasks to understand the nature of cognitive processes in children with autism. His graduate student, Amanda Moffitt, has been closely involved in the research. The topic is also of interest to David Beversdorf, MD, of the university's Thompson Center on Autism and Neurodevelopmental Disorders, who is researching pharmacological effects and stress.

John Kerns, PhD, an associate professor in the Department of Psychological Sciences, is examining schizophrenic performance. In particular, he is interested in their control of their behavior or what is termed executive function, and studies these processes in normally functioning individuals as well. Impressively, he has an article in Science magazine on this topic. Two of his students, Theresa Becker and Elizabeth Martin, have been heavily involved in his research, and a social psychologist, Bruce Bartholow, PhD, will join Kerns to extend the research to the effects of alcohol, a topic of special interest to other leading faculty in the department.

A new faculty member in the department, Keith Schneider, PhD, studies brain structure and function in relation to visual perception and, in one project, will be studying the underlying causes of dyslexia, a common reading disorder. He is also developing methods to take advantage of the inadvertent head movements subjects make in the MRI scanner, to sharpen the brain images.

Those are the faculty with the most expertise in imaging. Other professors have used behavioral and electrophysiological techniques and are now starting imaging studies. In the Department of Psychological Sciences, Steve Hackley, PhD, and Naveh-Benjamin are interested in memory in aging, Alzheimer's disease, and Parkinson's disease. I am interested in working memory – the small amount of information that can be held in the mind to carry out cognitive tasks. Dawei Li is a student who came from China with extensive neuroimaging experience and is helping with the memory research. Rouder plans to study perception and consciousness.

The facility is open to users from other departments, and Brick Johnstone, PhD, of the Department of Health Psychology, and Dan Cohen, PhD, of the Department of Religion, are working together on the role of spirituality on brain function.

The uses will not be limited to brain research, either. Members of the Department of Nutrition and Exercise Physiology, chaired by Chris Hardin, PhD, are interested in using the scanner to study body composition, cardiovascular function, and liver function in obesity and during obesity interventions.

Benefits to the Department and University

Bettencourt is thrilled about the effects of the brain imaging center. She notes that it "provides our faculty a sophisticated tool for answering their research questions. Already, it has encouraged collaboration across the department and the university." She believes that it should "attract additional quality faculty."

Indeed, Schneider, a beginning faculty member in the department, notes that the center "is a world-class facility that provides researchers one of the essential modern tools to help unravel the mysteries of the human brain. Its existence was one of the primary factors motivating me to come to the University of Missouri." The scanner room is equipped with a high-quality system to project images, a multichoice responses box that rests on the participant's chest, eye-movement tracking, and special headphones that work well in the scanner while deadening

2/25/2009

the mechanical noise.

The center is already proving quite important in maintaining the excellent federal funding record of the department, as this technique is now expected as part of many – or even most – grant proposals to be funded by the National Institutes of Health in this area.

Students are excited, too. Martin indicates that the center gives her "the opportunity to experience and learn increasingly indispensable research designs and methodologies" and says "it was actually a major deciding factor in my decision to attend Missouri for graduate school." Becker and Moffitt similarly note the extraordinary opportunities that it opens up.

The university is in for some exciting and rewarding times and an opportunity for researchers from different fields to meet each other, work together, and broaden their academic interests. In these fiscally difficult times, that is not a bad thing. One goal of the center is to generate enough research business that we will be in a position to afford to commission a work of art for the waiting room.

— Nelson Cowan, PhD, is Curators' Professor and director of the Brain Imaging Center at the University of Missouri-Columbia. Direct all questions and comments to <u>editorial@rt-image.com</u>.

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