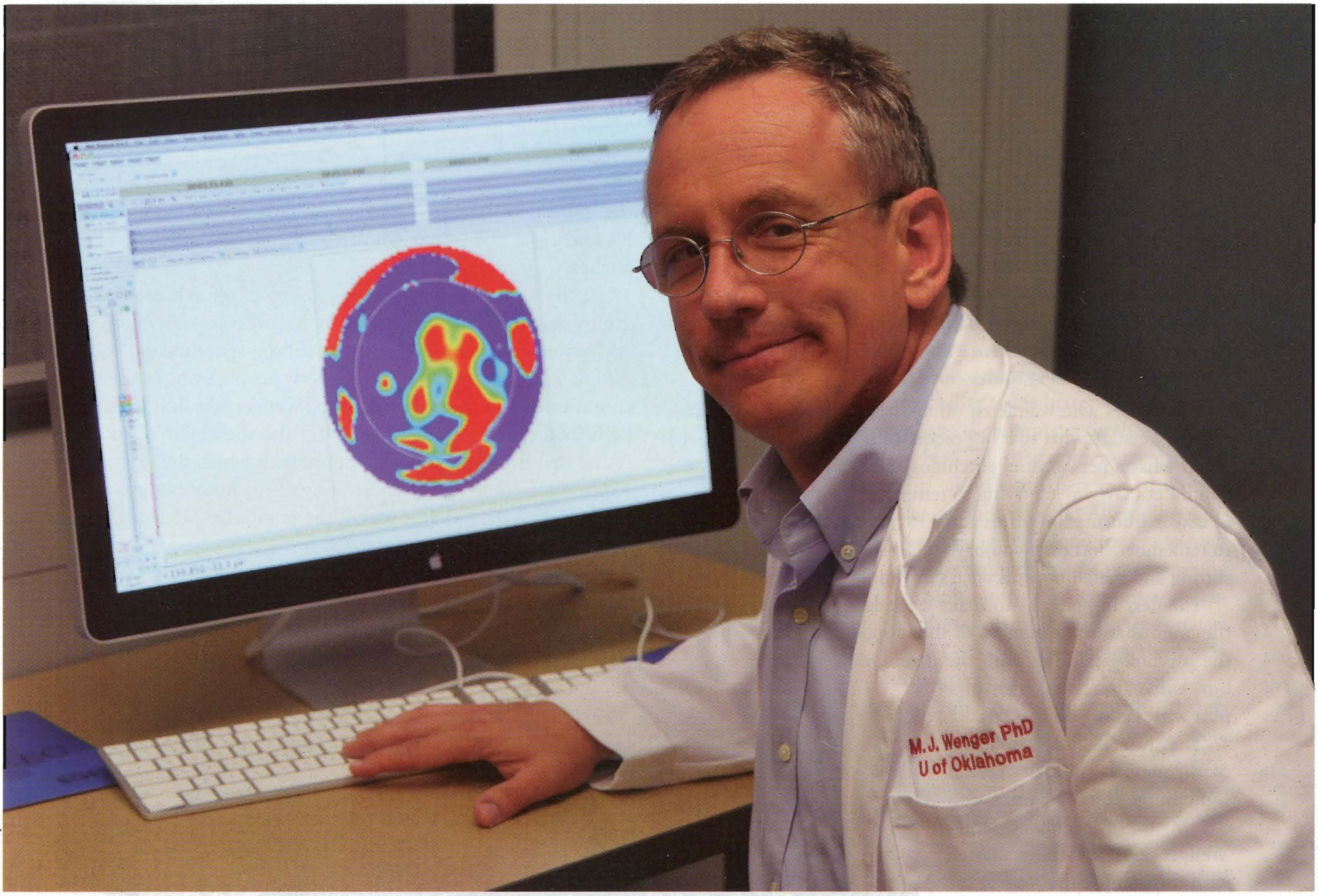
In the television crime drama "Numb3rs," brilliant but nerdy Charlie Eppes routinely upstaged his FBI-agent brother by using mathematical modeling to help the agency catch criminals. At the University of Oklahoma, real-life psychology professor and self-professed nerd Michael Wenger takes the same approach to solve even bigger mysteries—those within the human brain.

"I was trained as an experimental psychologist," Wenger says. "The way we develop a theory about something is to use mathematics. When we write out relationships mathematically, we make incredible leaps."

Some of those leaps include identifying early signs of Alzheimer's and discovering the hidden connection between iron intake and brain function. With a master's degree in engineering and a doctorate in experimental psychology, Wenger has long been fascinated with taking the complex and enigmatic processes of the brain and defining them with mathematical expressions. The titles of his many publications are replete with the multisyllabic terms one might expect from combined research in psychology, engineering and neurobiology, but Wenger compares his job with that of his next-door neighbor on the OU research campus.

continued



Robert Taylor

The Language of Science

Using mathematics, an OU psychology professor helps unravel the mysteries of the human brain—one equation at a time.

By Lynette Lobban

"My work is not that much different from what they do at the National Weather Center," he says. "To come up with an accurate weather forecast, they create these beautiful computational models of the atmosphere and use them to predict what is going to happen next. I use computer models of psychological experience and brain state to predict what I think will happen next under certain conditions."

For readers who wandered off at "brain state," Wenger elaborates. "We start with two big pieces of information. The first is about what a person does psychologically in terms of the task at hand. Let's say you are trying to remember something. You've got to take in information that is going to cue you as to what you want to remember, and then you have to do some kind of searching or sorting and matching with what's in your memory already."

The next big piece is to make a model of how the circuits of the brain that implement all of those operations work. "We pair the psychological ideas with the neural ideas in order to predict how the brain should then support what's going on in the task."

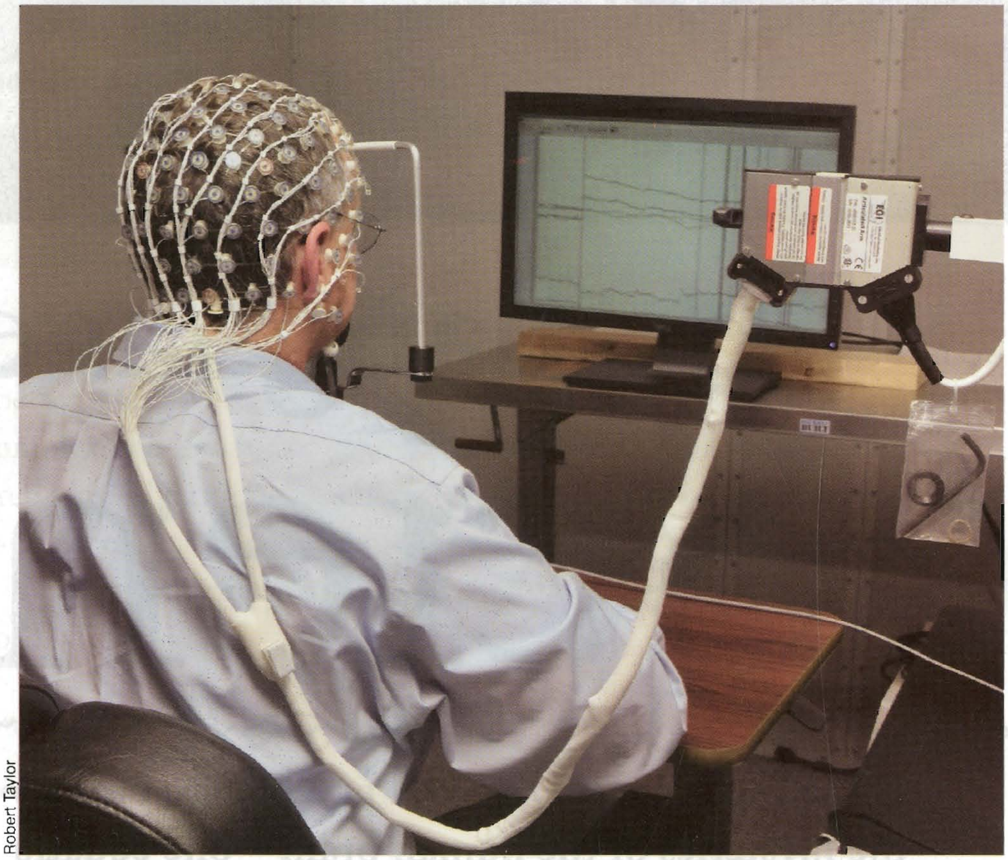
The fun begins when the mathematical model reveals something totally unexpected. In the Alzheimer's work, Wenger and associates started with the premise that one of the major things that is going on in early Alzheimer's is that the hippocampus—the seahorse-shaped part of the brain essential to memory—is basically falling apart.

"We said, 'OK, we know what the neural connections look like in the hippocampus. Let's set up a computer model of that circuit and then take pieces of it out,' " he says. "Next, let's predict where we should find the first sign of atrophy. We can test different theories based on the simulations we set up on the computer."

One of the biggest surprises revealed in the computer simulation was that the variable of time—how fast it took a subject to answer a question—was much more sensitive as an early indicator of Alzheimer's than the number of correct answers chosen. Wenger was able to test his theory at the Mayo Clinic's Alzheimer's Disease Research Center.

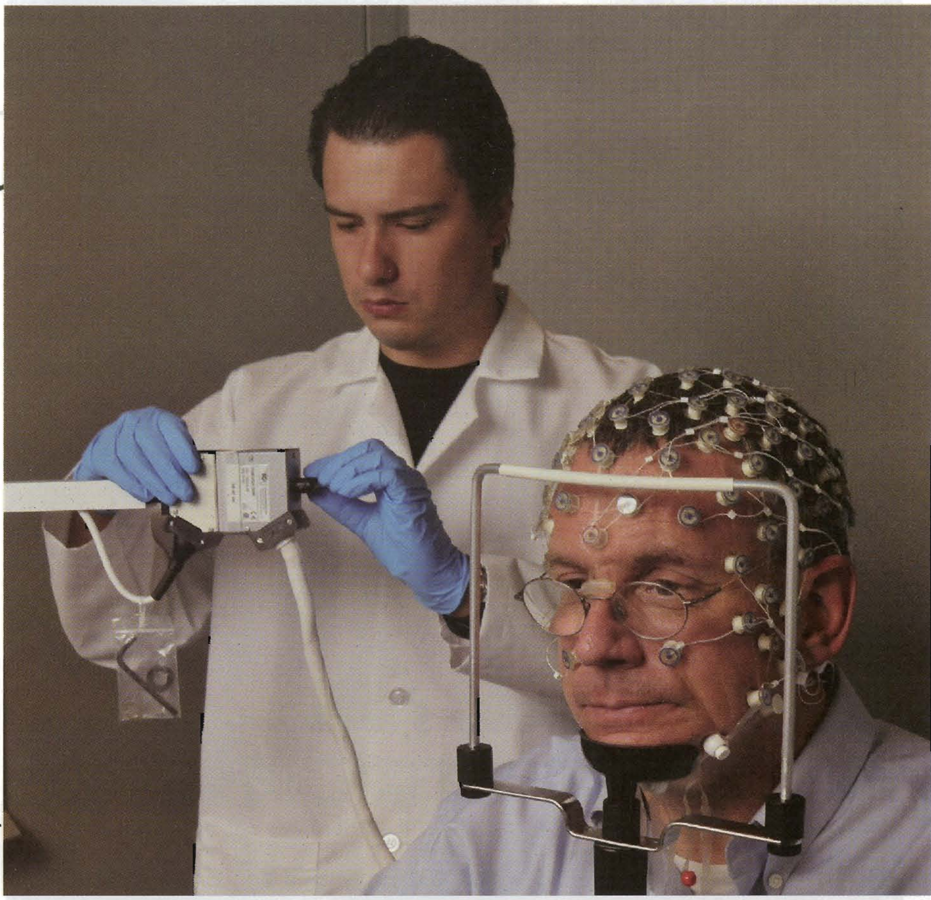
At the famed research site, he and colleagues studied a test group that had been identified as having very early stages of Alzheimer's and compared them to college-age students, healthy middle-aged people and healthy elderly people living in the same community. For the control group, Wenger not only had their performance on the memory test, but also their brain scans. "We found that if you looked at the speed with which the subject answered, you could detect the atrophy of the hippocampus much sooner," he says. "This is where the computer modeling really helped us."

He now is using similar data gathering and mathematical modeling on a very different project—looking at the effects of iron depletion, and subsequent repletion, in women of child-bearing age.



Robert Taylor

Michael Wenger dons an electrode cap as the scientist turns subject to gather data on brain function. Wenger, an experimental psychologist, uses computer modeling to help organize thousands of pieces of information. His research has uncovered new methods of identifying early signs of Alzheimer's as well as a link between iron intake and improved brain function.



Robert Taylor

Wenger, shown here with postdoctoral fellow Nick Altieri, compares his work to that of a meteorologist at the National Weather Center. Both disciplines utilize mathematical models to predict what will happen next.

The test group was comprised of approximately 250 women who worked on plantations picking tea.

"These women were typically very depleted in terms of iron," says Wenger, "and their ability to work quickly determines their income. So the ability to see better and work faster has a direct impact on their family."

Half of the women received an iron additive in their salt, the other regular iodized salt. All of the subjects were given blood tests at various times throughout the study, along with monitoring heart rates and other physiological data. The researchers used GPS devices to track the women's activity levels as they worked.

At the end of 10 months, the effects of the iron supplements were "astonishing." Wenger says the performance on the cognitive tests improved drastically for the women who received supplemental iron.

The next step was to develop mathematical models for what was going on in the brain during that time. Wenger began modeling a set of brain structures known as the basal ganglia, basically the hub for information processing.

"One of the reasons we chose basal ganglia is that the structures are highly affected by the level of iron in the blood. And one of the ways in which iron can affect the brain is by way of the myelin, the fatty wrapping around the neurons that's basically like the shielding on a cable. If that isn't intact, the signals don't make it along the cables," he explains.

"The other way it affects the brain is by way of neurotransmitters. If you don't have enough iron, you don't make enough of certain neurotransmitters, so even if the signal gets to the junction between neurons, you can't pass it across. Iron also provides a source of energy to the neurons, which they need to be active."

In June he joined forces with the research group at Cornell working to develop a method for using an electroencephalogram (EEG) to measure how efficient the brain is at using energy during cognitive testing.

"We can test the other hypotheses, the ones about the speed of transmission and the neurotransmitters, but we don't have a good way of relating the energy side of things," says Wenger. "We're going to see if we can use the EEG as a way to estimate how efficient the brain is in using energy. That will allow us to

Wenger says the entire project got off the ground when he fell off his bike, literally running into a professor on the Penn State campus. "I was riding my bike up the hill, he was riding down and, like typical academics, we weren't paying attention to what we were doing and collided," he recalls. As they were picking themselves up, the senior professor recognized Wenger and said, "Hey, I've been meaning to talk to you about something."

"He was in nutritional sciences, and I was working with mathematical modeling. He knew that I was interested in measuring perception cognition, and he wanted to do that in relation to iron deficiency." That initial conversation led to a joint project to measure changes in cognition of women with iron deficiency over a three-month period.

Around that time, researchers at Cornell were organizing a similar large-scale project with iron deficiency in India and asked Wenger if he would be interested in doing the cognitive perceptual measurements. The young psychologist jumped at the chance. He constructed six different tests that would help identify the pieces that go into perception and cognition.

The tests ranged from very basic-level perception—like how quickly someone could respond to the onset of a light—to more complicated tasks, like identifying similar faces amid distractions, which would measure recognition memory performance.

better mathematically model all the affects of iron on the brain."

Subjects will wear an electrode cap for EEG measurements while also being monitored for heart rate, temperature, volume of air processed and other biological data as they perform cognitive tests. "This will be one of the first times we will be able to put together body measures, brain measures and behavior measures," says Wenger.

The results could have a far-reaching impact on the medical community. Lack of dietary iron is one of the largest micronutrient deficiencies in the world, says Wenger. There are alarming rates of iron deficiency in women within the United States—sometimes as high as they are in developing countries.


Photo provided

Approximately 250 women took part in a large-scale project in India to measure the effects of iron deficiency on cognitive tasks. Wenger says the performance on the tests improved drastically for the women who received supplemental iron.

"It's incredibly easy to fix," he says, "but it rarely is fixed. Researchers primarily study this from the standpoint of anemia, but there has been increasing data suggesting that iron depletion has a massive effect on cognition. It affects memory. It affects perception."

The experimental psychologist says mathematical modeling has applications that are just beginning to attract attention across the OU campuses. "Scott Gronlund in psychology and I definitely have points of connection that we're both interested in exploring," he says.

"And Norah Dunbar [Department of Communication] and Matt Jensen [Management Information Systems] have started doing a bit of pilot work in the area of deception." Wenger clearly enjoys the challenge of creating a mathematical model for that.

"The first thing to do is to analyze the information that needs to be used in a lie," he explains. "You have to have the intention to lie, you have to plan the lie, and you also have this fact that you are trying to contradict. So you have all these pieces of information that you need to coordinate.

"I would start by constructing a model for how that process would have to be coordinated in the brain. There are circuits that are responsible for coordination of information, the basal ganglia, for example. But there are also reasonably well-defined circuits that manage conflict in information. So we would need to explore about how deception might be managed by these kinds of circuits."

Wenger would also like to take current projects, like the research in Alzheimer's and iron depletion and see how it relates to specific populations within Oklahoma, including Native Americans.

"I would like to be able to take what we have done with the demonstration of measurement and refine it. There's not a lot that can be done to prevent Alzheimer's, but there's hope that it can be slowed down if it can be identified early enough," he says. "The other thing that we'd like to be able to do is actually characterize what normal changes in memory are and distinguish between that and the early stages of dementia."

Wenger says oftentimes changes in the older brain are not really changes in memory, but changes in other things that mask the "expression" of memory. For example, muscle coordination gets slower, so older people are slower to think of a word or a name they know. He says this can look like a memory problem, but it is more just being slower at "looking through the files."

"The more you know, the longer it takes you to search your memory. The difference can be illustrated in the difference between going to a small community library and a major university library. There are a lot more volumes to search in the latter," he says. This is actually good news for seniors.

"In experiments, when you control for the amount of what people know in terms of their age, people in their 60s, 70s and 80s will actually outperform college students. So we could eventually make a mathematical model that will show what is normal versus early stage Alzheimer's."

For the next few months, Wenger will be busy analyzing the data from the Cornell project. "It's the first time this has been done," he says. "It's very exciting.

"It's also a lot of fun."

Lynette Lobban is associate editor of Sooner Magazine.