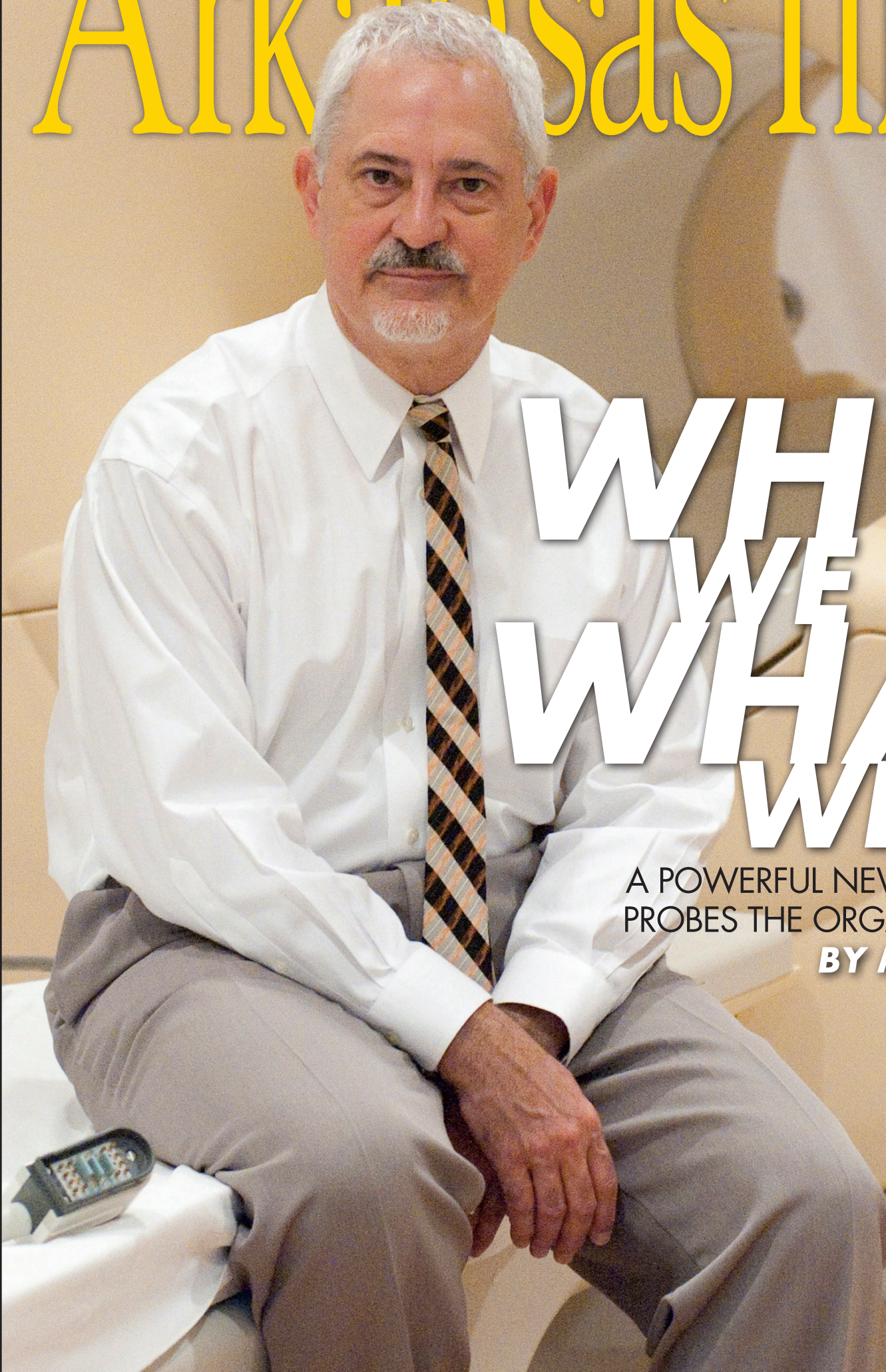


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WHY WE DO WHAT WE DO

A POWERFUL NEW TOOL AT UAMS
PROBES THE ORGAN OF THOUGHT
BY MARA LEVERITT
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MAN AND
MACHINE: Dr.
Clint Kilts and
UAMS's fMRI
machine.

A 'whole new day' in psychiatry

If you can think it, Kilts says, he can image it.

By Mara Leveritt

The pleasure Dr. Clint Kilts takes remembering his grandfather is evident. His genial face softens. The corners of his eyes crinkle. "He was a trickster," the neuroscientist chuckles.

Kilts' expression changes in countless subtle ways as he recounts how his grandfather, an oral surgeon, would pick him up on Sunday mornings when he was young, dressed as if for church. Kilts' parents were Catholic, his grandfather was not. Mass was not their destination.

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Instead, the pair would head to the racetrack, where grandfather would teach grandson how to handicap horses. When it was about time for Mass to have ended, they would return, stopping by the church on the way so that Clint could run in to pick up the weekly bulletin and go home with no one the wiser.

Or so the boy thought — until the day, years later, when his mother asked him how he enjoyed those trips to the track. “How did you know?” Kilts asked. His delight is obvious as he relates her reply: “Where do you think he took me on Sundays?”

Faces let us glimpse what’s going on inside a person. We intuit something about their thoughts and feelings by “reading” infinitesimal changes in their expressions. But Kilts delves deeper. He and his staff at the University of Arkansas for Medical Sciences will be watching changes inside people’s brains.

As the founding director of the school’s new Brain Imaging Research Center (BIRC), Kilts will command a powerful new, \$3 million fMRI (functional magnetic imaging resonance) system. When patients or research subjects enter the fMRI machine, he and his staff, seated at computers in an adjacent room, will be able to watch their brains as they respond to visual or auditory stimuli.

Kilts expects the fMRI to reveal a biological basis for many behaviors that, until now, have been vaguely classified as “mental illnesses.” His excitement is evident when he says, “We’ve never had such a tool before.”

“I’m trying to show some of the physicians around here that what we have here is like a cardio stress test that can show heart defects on an electrocardiogram. That came along several years ago, and it’s a great tool. Well, now we’ve reached that point in psychiatry. We have a tool that can see what’s happening in the brain. We can actually see the suffering in people.”

The fMRI machine is a tube, something like a space capsule. A person lies down in front of it and an operator slides him or her about half-way into it. As the subject lies very still, computers can track activity inside the person’s brain with pinpoint accuracy.

“I generally say, if you can think it, we can image it,” Kilts says. “That makes illness open to study in a way it never has been before. It’s a whole new day in psychiatry.”

The BIRC is the newest part of UAMS’ Psychiatric Research Institute (PRI) — itself less than two years old and one of just nine facilities in the U.S. devoted to psychiatric research, treatment and teaching. Dr. G. Richard Smith heads both the PRI and the school’s Department of Psychiatry. “Most hospitals,” he says, “can’t afford a facility like this.”

FUNDAMENTAL BREAKTHROUGHS

But psychiatry — and the need for it — is big at UAMS. With more than 100,000 visits a year, the Department of Psychiatry accounts for one-eighth of the hospital’s outpatient visits. Beyond that, many illnesses treated in other departments — such as those related to obesity — are viewed as having a psychiatric component.

Smith wants the PRI not only to excel at treatment, but to understand what goes awry in the organ that controls behavior. As he put it, “I felt that we have got to find out what’s going on in the brain.” Smith sees the brain, whose activities have remained obscure for so long, as one of medicine’s last frontiers.

One Little Rock couple, longtime supporters of the PRI, contributed \$1.5 million to house the BIRC (see sidebar). Smith then raised another \$3 million to equip it with an fMRI system twice as powerful as most and

‘Because people are scared.’

A Little Rock couple support psychiatry with money — and their names.

BY MARA LEVERITT

It was by no means a given that the new Brain Imaging Research Center at the University of Arkansas for Medical Sciences would bear the names of Helen L. Porter and James T. Dyke, the couple whose contribution of \$1.5 million helped to build it. They intended for their contribution to be anonymous.

But Dr. G. Richard Smith, the director of the school’s Psychiatric Research Institute, pressed the couple to allow their names to appear on the building. “He felt it was important to show that people in this community weren’t afraid to be associated with psychiatry.”

“We understood,” Porter says. “Because people are scared. Perhaps of all the kinds of illnesses, people are most afraid of having a mental illness.

“If you have cancer, you can get chemotherapy, radiation, and so forth. But they think, ‘If you have a brain disease or mental illness, what do you do?’ There’s a kind of panic and helplessness.”

Porter knew that sense of helplessness well. “When I was growing up,” she says, “my own mother would say to me that psychiatrists are crazy and people who go to them get no help.”

Like many people, her mother saw mental illness or emotional suffering as essentially a character flaw. Porter recalls, “She had a friend who was depressed, and she would say, ‘If she would get up and get out of the house, she would get over it.’ My mother had no idea what that woman was dealing with.”

Porter admits that she herself was in the dark about the possible ravages of trauma when, years ago, she and her husband learned that one of their three sons, then aged 10, was being sexually abused by a teacher. They dealt decisively with the situation, then, never thinking that their son might need help, expected life to return to normal.

But “normal” was not to be. The boy began using marijuana as a teenager, and eventually, Porter says, “alcohol

and drugs became his medications.”

“We were so naive, so ignorant back then,” she reflects. “We had no idea how to deal with it. Over the years he went through about 10 rehab clinics. And, of course, by that time, I’d gotten a lot of therapy too.”

Finally, their son went to what is now the PRI at UAMS. He got the help he needed, and Porter says, “He’s great now. He’s been sober for three years.”

She credits her son’s and her family’s ordeal with teaching her, as she puts it, “that what goes on in your brain can make you sick. For example, the experience of sexual abuse can make a person not able to function in society.”

She also learned, as she puts it, that, “Every family’s got something. Whether it’s a child with an eating disorder, or someone suffering with anxiety or depression, or someone coming back from a war with post-traumatic stress.”

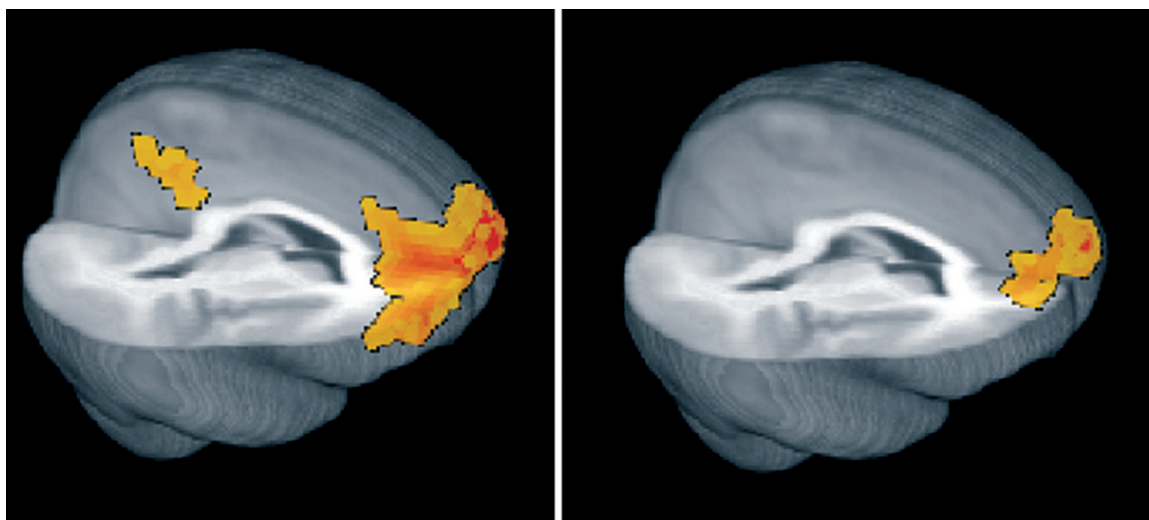
Still, many families guard such problems as unspeakable, much, Porter says, as when she was young, people would lower their voices to speak the word “cancer.” Porter and her husband agreed to lend their names to the new brain research building as a way of saying that it’s time for that era to end.

“There are plenty of people doing research on things like aging, heart disease and cancer,” she says. “But we know so little about the brain. We wanted to help fund this center because we think it’s just so hopeful.”

Her family’s experience also made Porter an advocate of the kind of psychiatry being practiced at PRI. “Have you seen the building?” she asks.

“It’s got all that glass out front. The interior is so open. And there’s that beautiful sweeping stairway. They acknowledge mental illness, but that place is about mental health.

“Everything about it says, ‘There’s nothing to be ashamed of here.’ Of course, there’s patient confidentiality, but the message is that this is not something to be hidden. You don’t have to be ashamed if your life is not going well. You can be seen. And you can get help.”



fMRI IMAGES: The image on the left represents a “healthy” brain. It shows how the medial prefrontal cortex (the large area shown in red and yellow), which is involved in emotional regulation, should be connected with the rest of the brain. The image on the right is of a brain with major depressive disorder, or depression, that has never received treatment.

matched only by one other fMRI in the state, that one also at UAMS.

The magnets in the BIRC’s machine produce a magnetic field 30,000 times stronger than that of the earth. That pull temporarily realigns the iron in the blood of a

person lying inside, and that allows computers to track the flow of blood as it moves about the brain.

When a thought or emotion activates part of a person’s brain, the flow of blood to that region increases. Being able

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FMRI

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to see that activity now makes the biology that underlies thought as tangible as the biology that underlies movement, breath, or procreation.

As building on the BIRC began, Smith went in search of a scientist who could direct it “to explore the relationships between the brain and complex human behaviors.” The search led Smith to Atlanta, where Clinton D. Kilts, Ph.D., one of the pioneers of brain imaging, served as a professor and vice chair for research in the Department of Psychiatry and Behavioral Sciences at Emory University School of Medicine.

But Kilts declined Smith’s invitation. “When Clint first came to visit, we were off in a trailer with a set of blueprints,” Smith recalls, “and the BIRC was just a hole in the ground.”

A very big hole. The room housing the fMRI machine had to be lined with two independent layers of copper and fitted with cushioning to control the vibration. The machine itself had to be lowered in with a giant forklift.

The building went up, Smith persisted, and in October 2009, Kilts surrendered an endowed chair at Emory to join the faculty at UAMS.

“He’s one of the nation’s experts,” Smith says. “He’s both down-to-earth and incredibly complex. He’s one of the most generative scientists I know. And he’s very interested in teaching, very collaborative. I think we’ll have some fundamental breakthroughs here.”

‘WHAT’S THE MATTER WITH ME?’

Breakthroughs are needed. In only the recent past have scientists begun to realize that many disabilities that were once labeled as psychological problems, mental illnesses or even moral failings actually arise from physiological irregularities in the brain. New imaging techniques, such as with the fMRI, are allowing psychiatrists to see where those irregularities lie, target them with medicines and other therapies — and often turn around lives that sufferers once considered hopeless.

But the field is young. Kilts feels a sense of urgency to produce research that will help people who are in pain and desperate — people like the woman who recently left an anguished message on his voice mail.

“She was begging for help,” he says. “She said, ‘What’s the matter with me? I don’t know why I’m letting cocaine ruin my life.’ It was an earnest plea. She was crying out as if she had cancer. She said, ‘I’ve lost everything, and I’ve lost it again and again, and it will eventually kill me.’”

Addictions are one of psychiatry’s most intractable problems. Kilts has determined that research into its causes and cures will be one of five main issues he wants the BIRC to address. His work with brain imaging will complement work already being carried out at the PRI’s nearby Center for Addiction Research.

Kilts told the woman caller that he could not answer her questions — at least not now. While Kilts hopes that he or “someone” will find a way to help her, he believes it’s more likely a cure for addictions will be available “for those who follow her.”

“Because I do think addiction is solvable,” he says. “This problem that has plagued society for thousands of years is solvable. Just think of the untold suffering it has caused and the social costs. It’s the leading cause of preventable death in the U.S.

“And then think that this technology is one of the major tools we have for solving it, maybe even within my lifetime,



BRIAN CHILSON

SEEKING ANSWERS: Dr. G. Richard Smith is the head of UAMS’s Psychiatric Research Institute.

or the time-frame of my career. That is the goal.”

HEADWATERS OF LIFE

Childhood, the period that Kilts calls “the headwaters of life,” will be another major focus of the BIRC’s attention. There are two big reasons for this:

First, the damage caused by childhood trauma cannot be understated. Kilts says, “There is not a psychiatric diagnosis that does not include a history of childhood adversity, whether that’s from abuse, neglect or some kind of physical trauma, such as from an automobile accident.

“It’s irrefutable. Early life adversity is a constant factor in all psychiatric disorders. It simply puts the developing brain on a different trajectory.

“We know, for example, that childhood maltreatment produces a specific response to stress, in both men and women. It persistently and perhaps permanently affects how a person responds to stress. It compromises that response, and that can lead to significant problems throughout life.”

He adds, “It is very rare when you see an individual who’s done something heinous who doesn’t have an early life history of maltreatment or traumatic brain injury. We look at aggression and domestic violence, and our response is usually prison or some other punishment.”

But such simplistic responses ignore the causes of a person’s violence, Kilts says. “We’ve been very complacent about being OK with being ignorant.”

Violence is just one response to childhood adversity. Depression, anxiety, addictions and obsessive-compulsive disorders are others.

(Trauma in later life, such as that experienced by soldiers in Iraq and Afghanistan, takes a toll too. “There is an awareness at the Veterans Administration Hospital,” Kilts says, “that this is going to be an immensely traumatized generation.”)

The good news about brains is that, contrary to what was once believed, they can often rebound from traumas, sometimes remarkably. They are “neuroplastic,” that is, able to restructure and reorganize themselves. And the even better news about children’s brains is that they are exceptionally so.

It is now believed that early treatment, when abuse,

neglect or physical trauma is first detected, can literally heal a brain, much as a broken bone can be healed if promptly and properly set. Brains that have gotten off-track can often be set right again.

It’s not that psychiatrists weren’t interested in brains. The problem was that the human brain is so protected, by both the skull and the blood-brain barrier, that examining its activity was almost impossible without inflicting harm on the subject. Technologies such as the fMRI have changed all that. Which leads to the second big reason that Kilts wants to focus on children.

“I want to study childhood adversities because we have this tremendous potential to intervene,” he says. “What we see with the fMRI could provide insights into how we should treat that child.

“We can understand how various treatments — behavioral, cognitive or pharmaceutical — work in a child’s brain, and by seeing how the brain responds to them we should be able to predict their outcomes. We’ll generate images and, instead of a therapy that’s one-size-fits-all, we’ll be able to tailor treatments according to how an individual brain responds.”

EAVESDROPPING

Kilts also wants to focus on the problem of childhood obesity. “We know it’s a habit-based behavior,” he says. “A lot of the theoretical models of obesity bear a lot of resemblance to drug and other addictions.”

And obesity — dare we say it? — is a huge problem in Arkansas. Kilts notes, “We rank number two in the nation in its rate of childhood obesity. It’s a leading cause of premature death, and it undermines quality of life. Yet — it’s unbelievable — we’ve never as a country done one study on childhood obesity. We need to understand how the brain codes it.”

Kilts wants to research why some people eat enough and stop, and others keep on eating. Is it because the parts of their brains that recognize satiation are different? Is it because food triggers different emotions? And what about anorexia and bulimia? Kilts suspects that what we call “eating disorders” may well be brain disorders.

“Pediatricians tend to think of obesity as basically a



PROBLEM SOLVER: Kilts believes the equipment can help cure addictions and obesity.

metabolic problem,” Kilts says. “I take that as a challenge. I say to them, ‘Let me show you what the organ that really causes the problem is doing.’ Within a year I think we’ll see how we code obesity in the brain.”

Kilts speaks often about the brain as if it were a biological thinking machine using code that can be cracked. “All we’re doing is eavesdropping,” he says.

At one point he explains: “Every human sensation, act, emotion, thought or belief is represented by a code of neural information processing.” At another: “The brain transduces every genetic and every environmental factor into something we can see and perhaps diagnose.”

As awareness of brain imaging spreads, its impact is being felt in fields as diverse as marketing, spirituality and law. Neuroscientists at several universities, for instance, have been imaging the brains of Buddhist monks to understand the effects of meditation on brain activity. Their results have lent credibility to the idea that practices such as meditation and mindfulness, or a sense of spiritual belief, can serve as what Kilts calls “protective factors” against some forms of illness.

But other applications, such as the use of fMRI services for lie detection or even to predict a person’s likelihood of committing a crime, have given rise to debate and some concern. Few would probably disapprove if a brain scan could reveal the intent of a terrorist. But predicting behavior carries risk.

J.W. Looney, a distinguished professor emeritus at the University of Arkansas School of Law, warned of some of those in the current issue of the UALR Law Review: In an article titled “Neuroscience’s New Techniques for Evaluating Future Dangerousness,” Looney wrote:

“As neuroscience develops and the related technology is perfected, calls for its use to predict future behavior will increase. This poses what has been called a ‘challenge to one of the central principles of Anglo-American jurisprudence: namely, that people are responsible for their behavior, not their proclivities — for what they do, not what they think.’”

Applying neuroscience to business has also provoked debate, as Kilts learned when he and others scientists at Emory formed Brighthouse Neurostrategies Group, in association with Emory, to provide businesses with

“unprecedented insight into their consumers’ minds.” By revealing consumers’ preferences as shown directly by their brains, a company researcher said, data from fMRI studies would let them leave behind less accurate tools such as focus groups.

That claim, plus the fact that some of the group’s research was underwritten by an Atlanta-based Fortune 500 company and the research was conducted in Emory’s labs, provoked an outcry in some quarters against the school’s involvement in the new field that was being dubbed “neuromarketing.” One critic complained, “It is wrong to use medical technology for marketing and not for healing.”

Kilts, who was scientific director of Brighthouse, prefers to call what he was doing “business neuroscience.” And, though he says he is no longer associated with Brighthouse, he adds, “I can honestly say I would not have done anything differently.”

“I did not do it for financial gain, but because I realized that core aspects of the world of marketing are not founded on any science. I took it from the point of being a consumer and looking at why we consume.”

What he underestimated, he says, “was the animosity some people have for business.” Research that his critics saw as an unethical application of brain science to selling, Kilts viewed as information that would empower consumers (by letting companies see what they wanted) and thus would allow businesses to better satisfy them. He remains interested in the topic.

“I have an article about to come out in the Harvard Business Review on how the brain handles strategy and decision-making. And I love it. Here’s this storied old business journal, and they’ve never had an article on neuroscience.”

“I saw it as an opportunity to inform the business brain at a novel level, because the more informed corporate decision-making is, the better off we are.”

THE SO-WHAT TEST

That seems to be Kilts’ attitude in general. Science has to help.

Referring to his planned research into addictions, childhood obesity, childhood adversity, and a few

other “strategic” issues, he says, “I can generate some amazing images out of this group of studies, and every time we do something, we’re the first in human civilization to see it.

“That’s really exciting, but we also have to pass what I call the so-what test. If what we produce is not something that reduces the burden of illness, we’re not fulfilling our mission.”

That burden is not an abstraction to Kilts. He tells students, “You have to be passionate about the human condition to do this work, and to be passionate you have to be personal.”

He traces part of his own passion to when he was 13 years old and had a close friend “who didn’t show up for school one day.” The friend didn’t come the next day, or the day after that, either. When asked, the boy’s parents only said vaguely that he’d “gone away.”

“Eventually,” Kilts says, “he came back, and I learned that he’d had his first brush with schizophrenia. And even though he was back, I could see that somehow he was gone. He was standing in front of me, but he was gone.”

That experience did not immediately steer the young Kilts towards psychiatry. At the time, he expected to become a dentist, like his beloved grandfather. But his grandfather dissuaded him.

He told the boy that, unlike horse races, dentistry was a lot of the same thing over and over again. He didn’t think Clint would enjoy that.

So Kilts pursued a Ph.D. in pharmacology at Michigan State University, then specialized in neuropharmacology at the University of North Carolina at Chapel Hill. He joined the departments of psychiatry and pharmacology at Duke University before moving to Emory in 1992.

Now, having long ago “stumbled” into his career as a brain researcher, Kilts recognizes that what he loves most about it is what his grandfather foresaw. “The simple fact is that no one’s done any of these studies,” he says. “Everything we do here is new.”

So the question arises: Is there some holy grail he’s going after, a mystery of the brain he’d like to solve, a discovery that could win him, say, a Nobel Prize in biology?

For a half second, Kilts looks embarrassed on behalf of the asker. But he answers quickly.

He names scientists, physicians and administrators around the UAMS campus, at Arkansas Children’s Hospital, and at the VA without whom the BIRC’s work could not be done. He lists essential grants from the National Institutes of Health, the Robert Wood Johnson Foundation and other funding sources. He explains that brain research is a “team science,” a field with little room for ego.

“This Brain Imaging Research Center is a huge commitment financially,” he says soberly, “and it’s going to require a huge expenditure of energy. I expect us to produce and I expect us to be judged. We should get a report card on the quality of our science. But ultimately, what’s important is what we give back here.”

One thing Kilts hopes the BIRC and the PRI will quickly give Arkansans is relief from the stigma that has for so long shadowed psychiatric illness. By connecting troubling behaviors to a troubled organ — the brain — he and Smith hope to free psychiatric illnesses from an unfair burden of shame.

More important, they hope to actually change troubling behaviors by changing troubled brains. Beyond that, Kilts says, “It would be a great day if we could put psychiatry out of business by developing models of prevention in early life that would relieve this state’s burden of illness.”