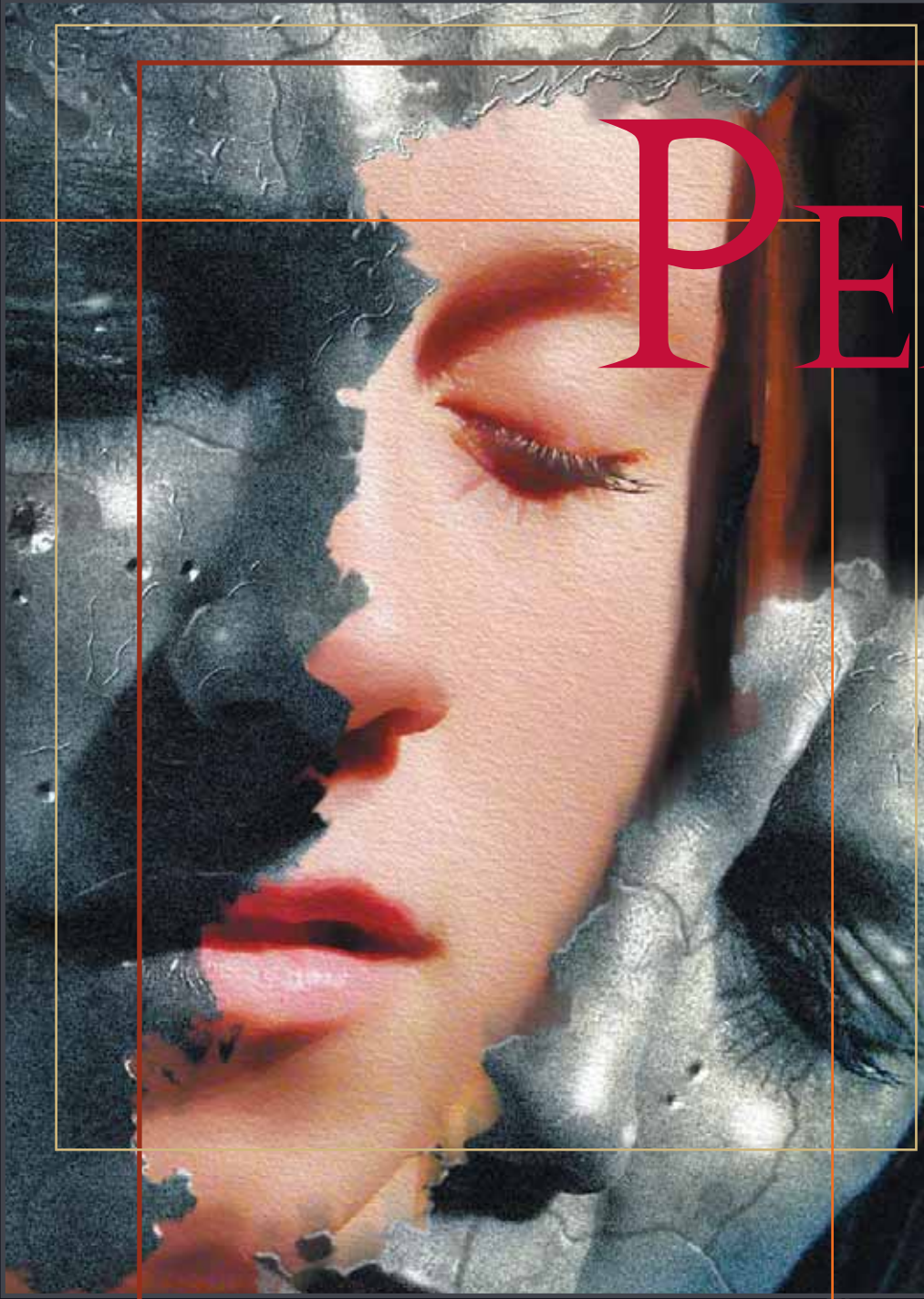


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DOZENS OF UF RESEARCHERS SEEK A BETTER
UNDERSTANDING OF THE MYRIAD OF FACTORS
THAT INFLUENCE HOW PAIN AFFECTS PEOPLE



IVING PAIN

BY MELANIE FRIDL ROSS

Whether it's the bite of the dentist's drill, the viselike contractions of childbirth or the crushing pressure of a heart attack, one thing's certain: Pain is commonly feared yet poorly understood.

The sensation may be universal, but the intensity with which it is felt varies widely, colored by past experience, anxiety, insomnia, cultural conditioning and fundamental biological or psychological makeup. Now research at the University of Florida is adding credence to the realization that factors such as age, gender, ethnicity and even our genetic wiring play an important role in pain perception.

No fewer than 50 UF scientists are involved in a campuswide boom in pain research. They are involved in more than 78 diverse research projects, many through three thriving pain centers based at the Health Science Center that account for at least \$12 million in federal grant money.

"There's just an enormous amount of research going on, everything from bench science with animal models and tissues to human outcome studies," says UF psychologist Michael E. Robinson, who directs UF's Center for Pain Research and Behavioral Health, part of the College of Public Health and

Health Professions. "We are really rapidly becoming one of the biggest universities in the nation to look at pain."

Experts say properly assessing and treating pain is a huge challenge. The National Institute of Neurological Disorders and Stroke reports that chronic pain afflicts nearly 90 million Americans. Pain is the number one reason patients visit physicians, and the second most-common reason to miss work, next to the common cold, Robinson says.

"It could certainly be argued that pain is the most prevalent and most expensive public health problem in the United States today," says Roger Fillingim, an associate professor at UF's College of Dentistry who teaches a graduate-level course on the neurobiology of pain. "It is estimated that more than 20 percent of the population is experiencing chronic pain at any given time."

The price tag is hefty: Medical bills, lost income and productivity, workers' compensation and legal expenses associated with chronic pain are estimated at well over \$100 billion a year — more than is spent on cancer and cardiac disease combined.

The interest comes at a critical time. Congress has mandated the first 10 years of this century the Decade of Pain Control and Research. And the agency that accredits U.S. hospitals — the Joint Commission on Accreditation of Health Care Organizations — now requires caregivers to monitor and document pain as a fifth vital sign, along with blood pressure, pulse, respiration and temperature.

Lured by the diversity of pain research at UF, Bob Zeziarski left the University of Miami a little over two years ago to direct UF's newly established Comprehensive Center for Pain Research, a cooperative effort of the McKnight Brain Institute and the College of Dentistry. One of the center's goals is the development of clinical and basic science programs in pain research throughout the Health Science Center. Zeziarski's specialty is the study of pain after spinal cord injury, but he also is seeking to bolster existing research programs in aging and neuropathic pain, cancer pain, musculoskeletal pain, visceral pain and orofacial pain.



ILLUSTRATIONS BY BUSTER O'CONNOR AND WALTON DALE

“There’s an interesting quote, ‘Pain is a sensation that everybody needs but nobody wants,’” Yeziarski says. “Pain can play a very protective role in one’s life. But in a chronic state, pain really serves no useful or biological purpose. It can severely compromise quality of life, and it can affect not only the individual who has pain; it can cascade throughout the family or work environment by negatively influencing those around the person with chronic pain.”

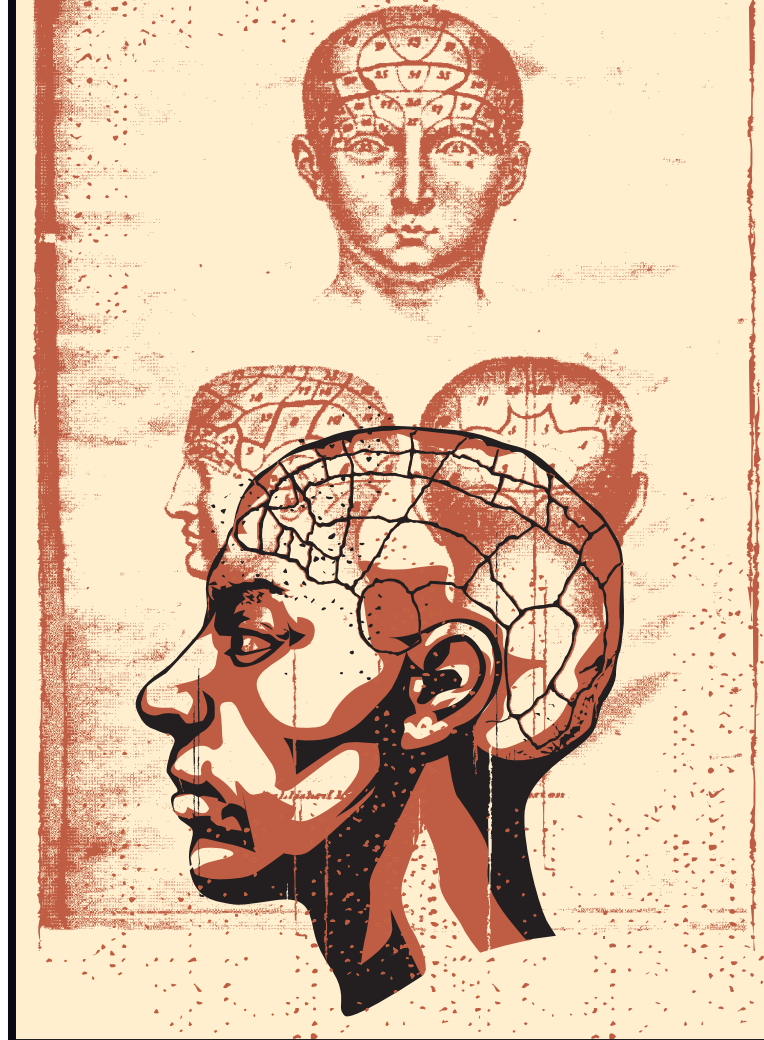
In Florida alone, a study conducted through the Florida Pain Initiative showed that pain is epidemic, and Floridians suffer more from chronic or recurrent pain than the national average.

Pain Paths

So what triggers pain? Picture an injury like a burn or a broken bone. In a flash, the damage activates a network of nerves, which send a warning signal to other nerves in the spinal cord that then transmit the information to the thalamus in the brain. From there, the alarm spreads to other brain regions. But everywhere along that pathway, changes can occur to alter the experience of pain, and pain responses among individuals vary tremendously.

“It will take a lot of research to learn why some people say ‘Ow’ at one level of stimulation, yet it takes a completely different level of stimulation to make another person say ‘Ow,’” says Robinson.

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Scientists have been striving for years to understand what causes many chronic pain conditions. They’ve learned a great deal about the anatomy, physiology and molecular biology of the pain system. Fillingim says his work is driven by a “biopsychosocial” model of pain, which holds that the experience of pain is sculpted by complex interactions among biological, psychological and sociocultural factors. These include mood, expectations, past pain history, age, gender and ethnicity.

“There has been increased interest in understanding all these factors so we can assess pain more accurately and treat pain more effectively,” he says.

UF researchers concede that teasing apart the underlying contributions of biology and society is no small task.

Women with chronic pain report slightly higher levels of pain than their male counterparts, for example, but the difference may be as much the result of how society

teaches men to handle discomfort as it is a consequence of biology.

“Clearly men and women are different in terms of how we raise them,” Robinson says. “We don’t understand how much of that is driven by social norms and how much of that is also driven by biology. There are huge social influences on men and women’s behavior. There are these stereotypes about how you should present yourself in public, and that includes the expression and admission of pain and seeking care for pain. Why should pain be any different?”

FILLINGIM AND HIS COLLEAGUES RECENTLY EXAMINED SEX DIFFERENCES IN RESPONSES TO PAIN-RELIEVING MEDICINES AND DISCOVERED A POTENT PAINKILLER APPEARS TO WORK BETTER IN WOMEN WHO CARRY A GENE ASSOCIATED WITH RED HAIR AND FAIR SKIN.



Studies have shown that when men and women report to clinics for pain control, men are far more likely to get higher doses of painkillers and women are more likely to get anti-anxiety drugs. Other gender stereotypes abound: Some people presume women are less tolerant of pain than men. In Western societies, the masculine role often demands that men maintain a “stiff upper lip,” stoic in the face of pain. Men, therefore, may be less willing to report pain when they feel it.

The rationale for studying gender differences in pain, Fillingim says, is that many of the most common chronic pain conditions are more prevalent among women than among men. Indeed, research suggests the burden of pain throughout life is greater for women than it is for men. Sex hormones such as estrogen may affect pain sensitivity, but most believe many factors interact to affect pain perception.

“Your stereotypes may be partly formed by differences in pain processing, but it’s clear your pain processing can be altered by your belief systems and your expectations and your stereotyped behavior,” Robinson says. “It’s possible we’re not treating people optimally because we’re not recognizing the sex differences we should, and we’re inappropriately recognizing sex differences that we shouldn’t.”

Robinson and colleagues are beginning to evaluate how physicians, dentists, nurses and other health-care providers are

influenced by such stereotypes. In one study, health practitioners will review various scenarios that feature male and female patients of various ethnicities experiencing the same degree of pain. Each provider then must decide whether to give each person pain-relieving medications. From the responses, researchers will determine how gender or ethnicity influenced their decisions.

Mean Gene

And then there’s genetics. Researchers now know pain isn’t just a symptom — it may have a genetic component.

“Now people are thinking more of pain as a disease,” Yezeriski says. “They’re starting to consider that some people can potentially be predisposed to chronic pain conditions, just as some are predisposed to cancer.”

Meanwhile, findings lend credence to the idea that scientists could someday maximize the effectiveness of prescription medicines for patients on the basis of specific genes. Fillingim and his colleagues recently examined sex differences in responses to pain-relieving medicines and discovered a potent painkiller appears to work better in women who carry a gene associated with red hair and fair skin.

“The ultimate goal would be to do a blood test on somebody,

look at their genetic makeup as well as other chemical, biological and physical characteristics, plug all that information into a computer, and the computer would print out a sheet that says, 'Okay, this drug, at this dose, is going to provide this patient the best relief from pain,'" Fillingim says.

Scientists also are considering whether ethnicity affects pain perception. In the health-care arena, discrepancies in pain perception or cultural attitudes about discomfort take on added import because they may influence whether someone seeks prompt medical attention. For example, physicians have long known that blacks wait longer to leave for the hospital when they have chest pain that might indicate a heart attack.

During the next five years, Fillingim's research team will study more than 300 blacks, Hispanics and non-Hispanic whites to gauge their responses to pain in a laboratory setting. They'll also look for differences in levels of one of the body's natural painkillers and a key stress hormone produced in response to pain, and study whether genes may play a role in the amount of pain reported.

"Given the increasing diversity of our population and the extremely high prevalence of chronic pain ... if we make the mistake of assuming that the pain experience is identical across all ethnicities and cultures, then we're going to do our patients a disservice," Fillingim says.

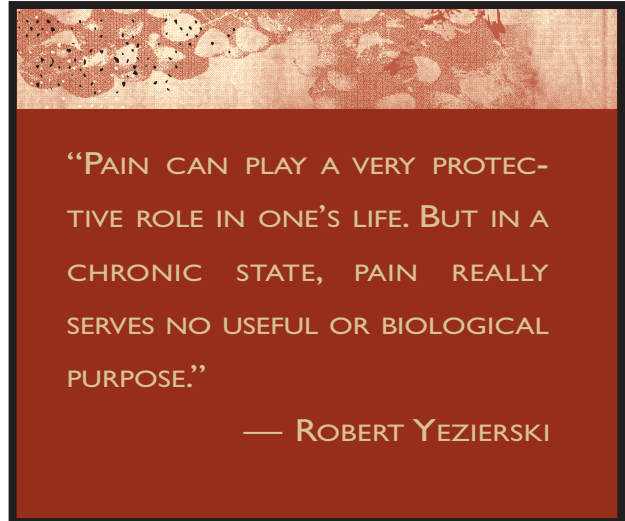
Although the past two decades have witnessed tremendous advances in the understanding of the neurobiology of pain, the development of new pain-relieving treatments has been disappointing, Fillingim says. Two thirds of cancer patients, for example, have poorly treated pain.

"I think if we're going to do better in the next 15 to 20 years, we're going to have to take a different approach," he says.

A better understanding of the molecular biology of pain could someday lead to gene therapy for pain management, Yeziarski says. And UF researchers are considering research projects aimed at identifying biomarkers for pain diagnosis and management.

For now, the most effective management strategy for chronic pain is a multidisciplinary approach that takes advantage not only of pharmacology or drugs but also psychological counseling, group therapy, physical and massage therapy, and exercise, Yeziarski says.

"A lot of different factors contribute to the pain experience," he says. "It's been demonstrated repeatedly that attacking pain from all these different dimensions usually leads to the most successful outcome." ✕



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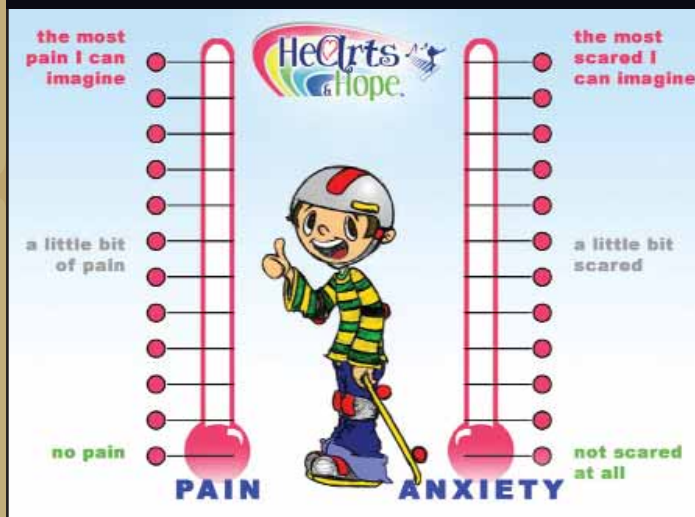
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Related Web sites:

<http://www.painlab.org>
<http://painresearch.ufl.edu>
<http://www.med.ufl.edu/rheum>

HOPE



Jay Klein avoided the Vietnam War, but not by choice. It was the winter of 1973, and, having pulled a not-so-lucky number seven in the draft lottery, the 19-year-old college student figured he was on his way. Yet when he reported for a routine physical exam at the New Cumberland Army Depot in Harrisburg, Pa., doctors didn't send him overseas like he expected. They ordered him to a urologist instead.

Forty-eight hours later he found himself on a different sort of front line altogether — battling testicular cancer in an era when few teens diagnosed with a malignancy of any kind survived.

After two surgeries and 18 months of chemotherapy, Klein suffered all the fears and uncertainty associated with treatment and survivorship in the 1970s. Three decades later, Klein is cancer-free, keenly aware of what cancer patients experience and committed to easing their pain, both psychological and physical.

As executive director of the HeArts & Hope Project, an innovative University of Florida program that will use streaming video-on-demand technology to deliver the arts to children hospitalized with cancer or sickle cell disease, Klein is helping lead a federally funded study designed to test whether the distraction of an “immersive multimedia environment” — videos on demand coupled with music in surround sound — can help alleviate pain and anxiety.

“I had procedures. I had a lot of uncertainty concerning my life and death, concerning pain,” Klein says. “But I have not seen anything like these children see today.”

Because their treatment is much more intense, their short-term physical pain and suffering is probably greater — and that may well translate into a harder long-term emotional recovery, he says.

The HeArts & Hope program began when Klein met UF pediatrician John Graham-Pole and Jill Sonke, director of the Center for the Arts in Healthcare, at a Tampa conference. Klein, a musician and the former program director for the Tampa Bay Performing Arts Center's educational initiatives,

sketched out his vision to Graham-Pole and Sonke: a virtual reality-like system that would seek to soothe a child's anxiety and discomfort, potentially reducing the need for opiate medications and even shortening hospital stays. A system they could scientifically test.

Klein and Graham-Pole pored over the scientific literature to learn other ways researchers had used physical space and the arts to distract patients from pain. Some had studied headphones in the operating room. Others had devised sophisticated 3-D virtual reality glasses for young burn patients.

They submitted a grant proposal for their immersive multimedia environment project and landed more than half a million dollars from the Department of Commerce. Matching funds from community partners and the UF Foundation brought the total to \$1.3 million.

The multidisciplinary HeArts and Hope team includes researchers from the College of Medicine's Department of Pediatrics, the College of Fine Arts and the College of Public Health and Health Professions. They are collaborating with artists and technology partners from around the nation to develop a network of streaming video broadcasts and video-on-demand for more than 200 children and adolescents treated at Shands Children's Hospital for cancer and sickle cell disease over the next three years. The images will be projected on 21-inch flat-screen monitors mounted on swing-arms, enabling patients to keep the equipment as close as they'd like.

“(After a cancer diagnosis) all of a sudden everyone wants to play violins and harps, and we understand that relaxation is a good thing, but we also are finding out from the children what is comforting to them, and that may break a lot of assumptions in our adult world,” Klein says. “These kids may very well want to rock.”

The concept of distraction is the theory behind the approach, Graham-Pole says.

“There's a limited number of pain pathways or nerve fibers from the site of the pain to the brain,” he says. “If you can distract the person from these pathways to be aware of something else with their mind, then they will be less aware or even not aware of the pain. Music we know works very well; so does laughter. We know physiologically they both cause you to release endorphins, essentially the body's morphine.”

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