Reprinted Publication: TMS Therapy

Beyond Prozac
The Oprah magazine, May 2010

The attached article discusses several treatment options for depression, including TMS Therapy. NeuroStar® TMS Therapy system is the only TMS Therapy device cleared in the United States by the FDA for the treatment of depression.

NeuroStar TMS Therapy is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode.

Efficacy for NeuroStar TMS Therapy was established in a controlled clinical trial comparing active treatment with the NeuroStar TMS Therapy system to an inactive device. Patients treated with active NeuroStar TMS Therapy received an average reduction in their depression symptom score of 22.1% compared to a 9% average reduction in patients receiving inactive treatment.[1] Patients treated with NeuroStar also experienced significant improvement in anxiety and physical symptoms (such as appetite changes, aches and pains, and lack of energy) associated with depression.[2]

In an open label trial where all patients received active NeuroStar TMS Therapy, approximately 1 out of 2 patients treated experienced significant improvement in depression symptoms. Approximately 1 out of 3 patients treated with NeuroStar TMS Therapy experienced complete symptom relief at the end of six weeks.[2]

NeuroStar TMS Therapy has not been studied in patients who have not received prior antidepressant treatment. Efficacy has not been established in patients who have failed to receive benefit from two or more prior antidepressant medications at minimal effective does and duration in the current episode.

The most commonly reported side effect related to NeuroStar treatment was headache or scalp pain during the treatment session. This side effect was generally mild to moderate and occurred less frequently after the first week of treatment.[3] As with any antidepressant treatment, patients should be monitored for symptoms of worsening depression.

1) Data on file.
2) Demitrack, MA, Thase, ME. Clinical significance of transcranial magnetic stimulation (TMS) in the treatment of pharmacoresistant depression: synthesis of recent data. *Psychopharm* Bull. 2009, 42(2): 5-38.
3) Janicak, P, et al. Transcranial Magnetic Stimulation (TMS) in the Treatment of Major Depression: A Comprehensive Summary of Safety Experience from Acute Exposure, Extended Exposure and During Reintroduction Treatment. *Journal of Clinical Psychiatry,* February 2008.

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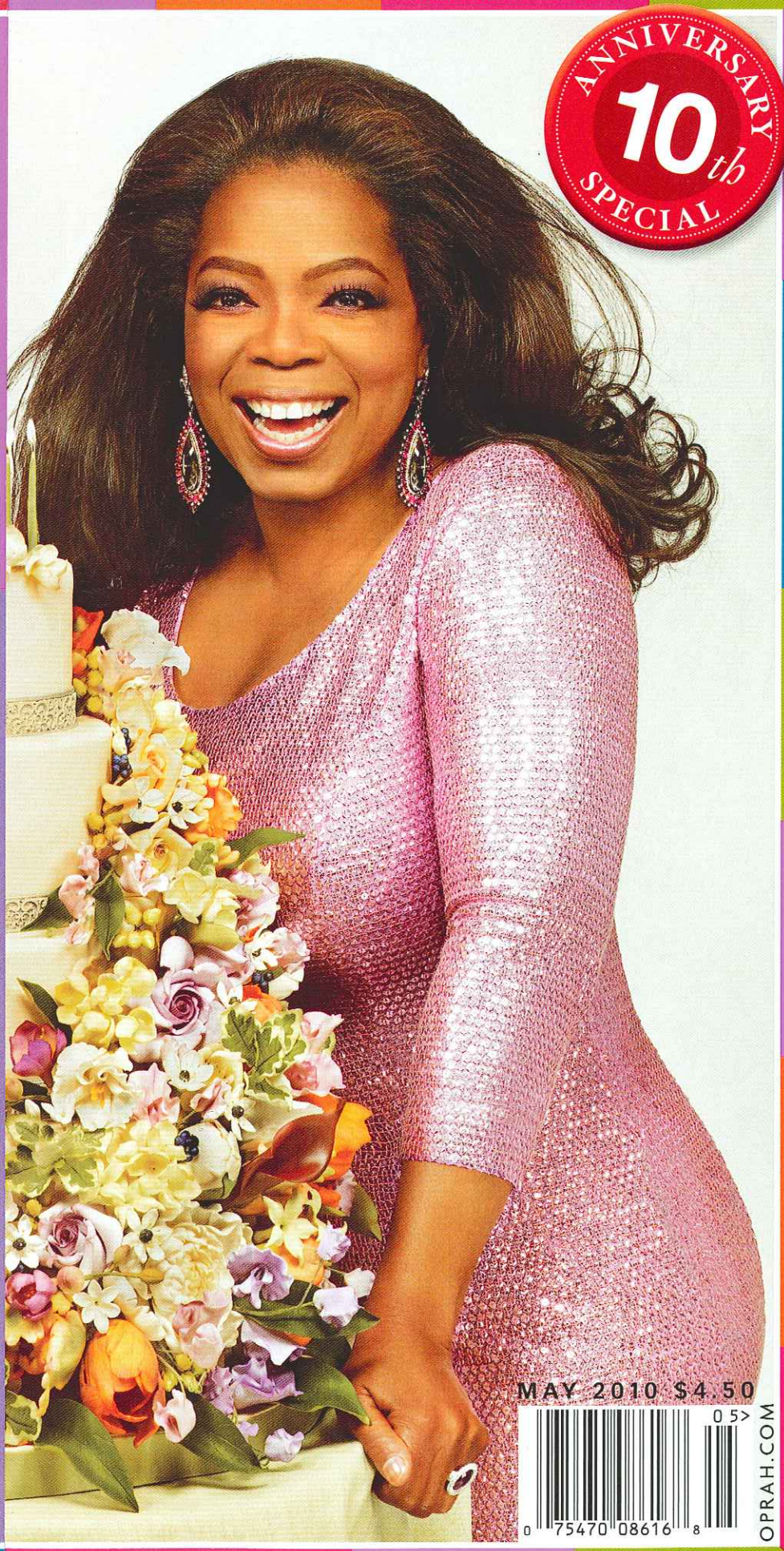

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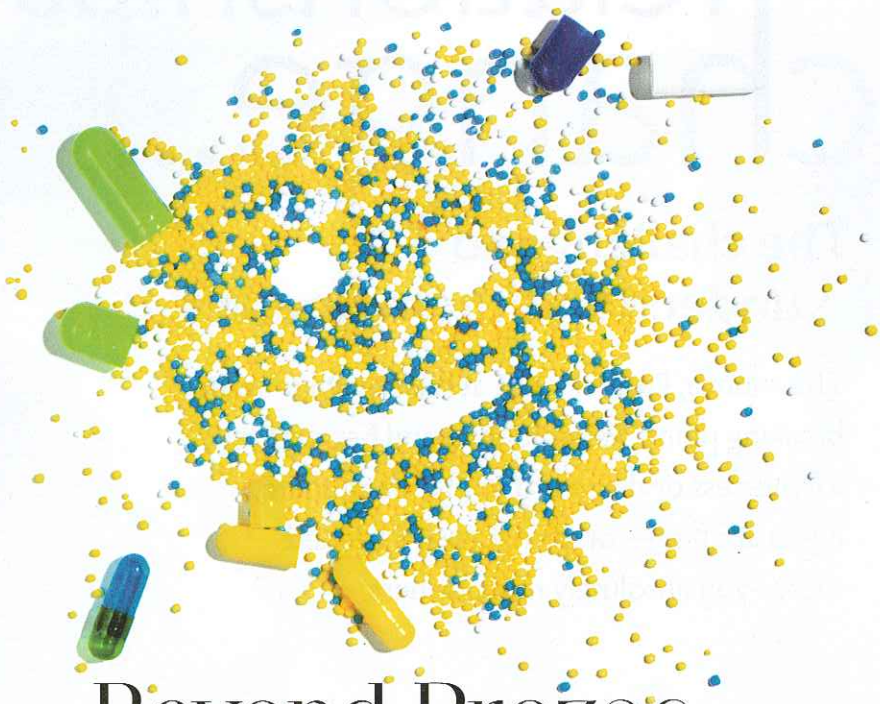
Srivastava says. Eventually, IPS technology could even be used to create entire transplant-ready hearts, though that level of engineering is likely at least 20 years away. "Creation of an entire heart from a patient's own cells will represent the ultimate in personalized medicine," Srivastava says. "The replacement organ will be genetically identical to the patient and will not suffer the risk of rejection, and patients will no longer have to die waiting for an organ donor."

Kenneth Chien, MD, PhD, director of the Cardiovascular Research Center at Massachusetts General Hospital and a professor of stem cell and regenerative biology at Harvard University, is leading one of several global heart patch research efforts. He believes that clinical work on a patch could begin within five years—though he notes that the first studies are likely to focus on safety (stem cells can cause tumors if left to divide unchecked) and technical challenges (including how to get new muscle to beat in time with the rest of the heart).

But Chien is confident that these and other problems will be solved. In the meantime, both he and Srivastava note, IPS cells may help revolutionize drug development for patients with inherited cardiac disease. Until now, scientists seeking to treat people whose heart problems are caused by genetic mutations had only one option: to breed a mouse or rat with the same mutation, and then try to cure the animal with drugs. IPS cells could offer a faster and more efficient way to test potential treatments.

By taking skin cells from patients with genetic heart problems and turning them back into stem cells, scientists would be able to create a pool of the very same dysfunctional heart cells they seek to fix. Multiplying those cells in the lab would allow them to test hundreds of drugs, harmlessly, until they identified one that could slow or stop the disease.

"I think of cardiac stem cell research like a river," Chien says. "Twenty years ago, we couldn't even see how deep or wide the river was. Now we can not only see the bottom but we're starting to build a bridge to the other side."



Beyond Prozac

Nearly 25 years after the Prozac revolution, scientists are seeking faster, more effective ways to loosen the grip of depression. **BY ANNIE MURPHY PAUL**

IMAGINE YOUR DOCTOR HAS JUST DIAGNOSED YOU WITH depression. She sits down to write you a prescription for an antidepressant, but not before she performs a simple blood test that tells her exactly which medication will work best for you. You take a pill in her office, and within two hours your mood is already lighter.

Or suppose you decide to go into therapy—except in addition to seeing a shrink, you also check in with a computer program that leads you through a series of depression-relieving exercises. Or let's say drugs and therapy have failed to relieve your symptoms, so your psychiatrist suggests an alternative treatment. He positions a device on your scalp that's designed to stimulate activity in certain areas of your brain, and after several weeks of sessions, your depression lifts.

SUCH SCENARIOS MAY SOUND FAR-FETCHED, BUT IN FACT THEY may not be long out of reach. And they represent a new generation of research that, according to Andrew Leuchter, MD, professor of psychiatry and biobehavioral sciences at UCLA, may offer "treatments that are a marked improvement over what's available now."

Today many people with depression are prescribed drugs (like Prozac and Zoloft) that belong to a family of medications known as selective serotonin reuptake inhibitors (SSRIs). But these *(continued on page 158)*

drugs have drawbacks. One is that only about 30 percent of patients see improvement from the first SSRI they take; others must try another medication, or two or three, before they find one that does the trick. Leuchter is working to eliminate the trial and error by using biomarkers—signals from our bodies that can indicate whether a treatment will be successful. Right now one of the most promising biomarkers is changes in brain activity. By comparing a brain scan taken immediately before a patient starts an antidepressant to a scan conducted just one week later, Leuchter says he can predict with 74 percent accuracy whether the medication will ultimately make the person well. The future may bring an even speedier shortcut: a blood test that would match a patient with the right drug based on her genetic makeup, before she ever takes a pill.

The other drawback to SSRIs is that they can take up to 12 weeks to make people feel better. That's because the drugs work in part by setting off a chain of neurochemical events that eventually regulates brain levels of glutamate, a neurotransmitter that improves communication between neurons. A drug that targets glutamate levels directly could improve mood much faster. One drug that has been shown to do so is ketamine, which is currently used as an anesthetic.

In one experiment, researchers at the National Institute of Mental Health (NIMH) administered an intravenous dose of ketamine to a group of people with depression. "Less than two hours later, the participants reported feeling better. Within 24 hours, they had achieved the same level of depression relief that people on SSRIs get in approximately six weeks," says Carlos Zarate, MD, a scientist in the Mood and Anxiety Disorders Program at the NIMH and lead researcher on the study. "When it comes to the speed of depression treatment, that's like breaking the sound barrier." However, ketamine can also temporarily distort sensory perception, so Zarate and his colleagues are hoping to create newer versions that would be just as effective but safer.

> Voice analysis software can gauge a patient's mental state based on nuances of her speech.

OF COURSE, EVEN THE BEST MEDIcations are often not enough to combat severe depression—for which psychotherapy is also an important part of the recommended treatment. The trouble is, many patients never get therapy. "In many communities, there is a shortage of trained therapists," says Jesse Wright, MD, PhD, director of the University of Louisville Depression Center in Kentucky. "And therapy can be expensive. But in the future, a computer may help solve these problems."

In computer-assisted therapy, or CAT, sessions with a human therapist are supplemented with the use of interactive software. The computer might show you a video of a woman who is depressed and demonstrate how her low mood is perpetuated by her excessively negative thoughts. The program would help you identify these types of thoughts in your own life, and lead you through exercises designed to get you thinking more clearly and positively.

Computers may also help doctors screen people at risk for depression, via voice analysis software that gauges a patient's mental state based on nuances of her speech. "Depressed people tend to talk in characteristic ways; their speech is quiet, slow, without a lot of variety or emphasis," explains Alex Pentland, PhD, a professor at MIT who helped develop the software. After analyzing thousands of samples of depressed patients' speech, Pentland and his colleagues created a program that recognizes cues only a very experienced clinician would pick up. He predicts that the software will one day be used to "listen over the shoulder" of healthcare providers on phone calls with patients, issuing an alert when it identifies the warning signs of depression. *(continued on page 160)*

WHAT WILL THEY THINK OF NEXT?

CONTACT LENSES THAT PERFORM HEALTH CHECKUPS You may soon be able to check your blood sugar with the blink of an eye. The contacts of the future may contain sensors that measure biomarkers on the surface of your eyes—for instance, blood glucose or cholesterol levels—giving patients an easy way to monitor their health, says Babak Parviz, PhD, associate professor of electrical engineering at the University of Washington.

WHEN WE MIGHT SEE IT Five to ten years. Parviz's team has created some of the lenses' main components and is now testing the sensors. "Extremely complex microsystems must be integrated for this to work," he says, "so it's likely at least five years away." —*L.D.*

FOR MANY PATIENTS WHOSE DEpression doesn't respond to medication or therapy, the treatment of last resort was once electroconvulsive therapy (ECT). While effective, ECT can cause serious side effects, including memory loss. But a new generation of brain stimulation therapies is beginning to offer relief from intractable depression with fewer risks. "In the same way that cardiologists use pacemakers to correct abnormal heart rhythms, we're now beginning to use brain stimulators to correct the neural circuitry that's causing the psychiatric disorder," says Sarah Lisanby, MD, director of the Brain Stimulation and Therapeutic Modulation Division at Columbia University Medical Center in New York.

One therapy offered at Lisanby's clinic is transcranial magnetic stimulation (TMS). TMS delivers mild, painless electrical signals to the prefrontal cortex through a plastic-coated wire coil placed on the head. "The treatments stimulate nerve cells in a region of the brain called the prefrontal cortex," says Lisanby. "This area plays an important role in mood regulation, and it's often less active in people who are depressed." Scientists are also exploring how similar but more invasive technologies—such as vagus nerve stimulation and deep brain stimulation—might also be effective in alleviating treatment-resistant depression.

"In the past, our options for people with the most severe forms of the disease were very limited, but we're already able to offer a wider variety of safer choices," says Lisanby. For patients who have lived with the darkness of depression, such treatments will mean a bright new day.

The Big C: Customization

What if a simple test could detect cancer in its earliest stages—and reveal exactly which treatment would have the best chance of curing you? Welcome to the age of personalized medicine. **BY LAURA BEIL**

FOR DECADES, SCIENtists thought of cancer as simply a disease of good genes gone bad. Whether a person's DNA contained inherited mistakes or became damaged as cells went about their daily business, these glitches allowed cells to multiply unchecked. If they could find a way to stop the cells from reproducing, scientists assumed, they could cure the cancer. But today it's clear that the mechanisms behind the disease are far more complex. Oncology researchers have discovered that a tumor's growth is as much a product of its surrounding environment as it is of genetics. Research has also shown that even when two people have the same type of malignancy, the cellular changes that cause their tumors may be unique to each patient.

Although such findings suggest there may never be a universal cure for cancer, they have paved the way for more precise screening tests and more effective treatments. "We're on the brink of genuinely changing cancer treatment for the better," says Razelle Kurzrock, MD, head of the department of investigational cancer therapeutics at the University of Texas M.D. Anderson Cancer Center in Houston.

Already, targeted therapy—medications aimed at specific cells with certain mutations or other characteristics—is being used in some cancer treatment centers, and it will only become more common as the decade goes on. "In the past five years, we've realized that there's no 'one size fits all' when it comes to cancer," says Eric Winer, MD, director of breast *(continued on page 164)*