

Arthritis drug may treat bipolar disorder

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By Marina Pisano

They may not have an athletic or artistic bone in their bodies, but they are convinced they can win a marathon or paint a masterpiece. Feeling smarter, more creative and more important than others, they relish their high-energy levels and bask in feelings of euphoria.

For people going through a manic cycle of bipolar disorder, pronounced changes in mood and energy go way beyond the usual ups and downs people experience. Untreated, the illness can cause suffering, damage relationships, affect jobs and in severe cases result in suicide.

But while bipolar disorder is treated successfully in many patients through a combination of medications and therapy, not everyone benefits from the mood stabilizers now used. [Psychiatrist Jair C. Soares of the University of Texas Health Science Center at San Antonio](#) is examining what he calls a "long shot."

Soares is conducting a clinical trial of Celebrex or celecoxib, a popular drug used by millions for acute pain and inflammation associated with rheumatoid arthritis and osteoarthritis. Although not approved by the FDA for treating bipolar disorder, he thinks Celebrex holds promise and is enrolling San Antonio-area volunteers with bipolar disorder, ages 18 and older, for a 12-week study.

Those interested can call (210) 567-0781.

Bipolar disorder affects more than 2 million American adults a year, according to the National Institute of Mental Health. It can develop in childhood or adolescence and often runs in families, passed on through a combination of genes. It requires lifelong management. Drug and alcohol abuse can occur with the illness.

In the ongoing search for safe, effective treatments, "there is preliminary evidence Celebrex will work, but it doesn't come from controlled studies," says Soares, chairman of the division of mood and anxiety disorders at UTHSC. "If it turns out that it helps, that will be a very important development."

With a \$300,000 grant from the Stanley Medical Research Institute, Soares plans to enroll 80 adults over the next three years in a randomized, placebo-controlled, double-blind study. Half the patients will receive a placebo, half the Celebrex. Doctors and patients won't know who is taking which pill.

After six weeks, the blind will be broken to assess through mania and depression rating scales how patients have done. Study volunteers who respond to the Celebrex go on for another six weeks to see if the benefit is sustained. Those who don't respond to the medication don't continue. Volunteers who do not respond to the placebo get Celebrex for the next six weeks. Those who respond to the sugar pill — researchers say that does happen — do not continue.

The study is open to people with Type I bipolar (recurrent mood cycles with full-blown mania) and Type II bipolar (hypomania, milder episodes of mania alternating with depression). Volunteers receive a free diagnostic interview, a physical and routine blood tests. Medication is free. Volunteers are compensated for their time.

Soares explains that lithium, a mood stabilizer that has been around for a long time, helps many with bipolar disorder control their manic episodes. Other patients do well on Depakote (valproate), an anticonvulsant approved in 1995 for treatment of mania. Zyprexa (olanzapine), an

atypical antipsychotic, is used as well.

Recently, the FDA approved Lamictal (lamotrigine), a newer anti-convulsant, as a mood stabilizer. It helps more in the depressive phase.

Soares, co-editor of the international journal *Bipolar Disorders*, finds good reason to believe Celebrex will work. Inflammation in the body, as seen with arthritis, is related to increased levels of proteins called prostaglandins. With depression and bipolar disorder as well, levels of prostaglandin are abnormal over time. Giving patients Celebrex, which inhibits its production, may help.

In the study, Celebrex will be added to medications patients are already taking. "Basically, these are patients who despite available treatments haven't responded," Soares says. Study participants will be apprised of possible side effects with Celebrex, including stomach upset. People with pre-existing kidney conditions may have problems with it.

Treatment of bipolar is a difficult balancing act aimed at controlling the mania and depression through a combination of mood stabilizers and antidepressants. Not all patients respond well to a drug, and it takes time to get them stabilized.

In fact, the approach to treatment is still evolving as demonstrated in the research of Lori Altshuler, a professor at the University of California at Los Angeles Neuropsychiatric Institute, whose findings appear in the July edition of the *American Journal of Psychiatry*.

It is part of "long-standing clinical lore," Altshuler says, to stop giving patients antidepressants once their symptoms of depression improve and just keep them on mood stabilizers. "The

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concern has been the antidepressant could precipitate a manic episode even if you're using a mood stabilizer."

But after seeing patient after patient relapse when she used that approach, Altshuler decided to conduct a study. She looked at 84 people with bipolar depression whose symptoms of depression improved when they were treated with an antidepressant along with a mood stabilizer. Roughly half the subjects were taken off the antidepressant within six months of remission, while half kept taking it.

One year after symptoms improved, 70 percent of those who discontinued taking antidepressants had a relapse of depression, compared to 36 percent of those who continued taking antidepressants. There was no increased risk of manic relapse in the people taking the medication for one year.

Altshuler hopes the study affects how clinicians treat bipolar patients. But she says some patients don't respond well to

antidepressants and do switch into mania. And with rapid cyclers who switch moods back and forth many times a year, antidepressants may increase cycling. "This is trickier to treat than unipolar depression," she says.

Tricky and intriguing. The paradox of bipolar disorder is its association with both highly creative achievements and destructive behavior. Mozart, Napoleon, Vincent Van Gogh, Winston Churchill and a long list of writers, artists, actors, musicians, filmmakers and other notables, deceased and living, are listed on various bipolar Web sites.

While people riding the "high" of a manic episode frequently feel elated, energized and creative, Soares has seen the dark side of the cycle.

"If it becomes full-blown mania, it can become very disruptive. People can't think straight. They start things and don't finish them. They may develop outbursts and become violent. Someone may

become sexually indiscreet, hypersexual, and do things he or she regrets and destroy family life. One patient liked to race the police at 90 miles an hour. He found that immensely entertaining, but it would have serious consequences afterward."

On the depression side, up to 20 percent of people with bipolar disorder commit suicide. In the depressed state, "They don't eat. They have no energy to do anything. They see no point in living," Soares says. "Some patients have mania and depression at the same time, making it worse. They have the depressed state of mind and the energy boost of mania."

In all, it is a very serious mental illness, Altshuler says, which makes the search for improved treatments all the more compelling.

"It would be great if we could find the ideal mood stabilizer that could treat both the mania and the depression — one drug. But as of yet, it eludes us."