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MINDSCAPES

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Initiatives at the Forefront of Treating Major Depressive Disorder

Mass General researchers pursue breakthroughs in diagnostic tools and novel therapies

Doctors today often treat major depressive disorder (MDD) by trial-and-error, looking for one drug or combination of treatments that will combat its debilitating effects. But there is still no “magic bullet” for treating MDD. Now, in their intensive and pioneering quest to improve treatment options for depression, researchers at the Massachusetts General Hospital Depression Clinical and Research Program (DCRP) are identifying diagnostic tools and novel therapies that hold great promise to deliver better results in less time.

Despite the deepest federal funding cuts in years, DCRP researchers are determined to maintain that role, with an array of more than 40 projects under way supported by more than \$3 million in funding and a full-time staff of 30. A few of these projects are highlighted below.

GIANT STEPS TOWARD MORE EFFECTIVE TREATMENTS

One study, dubbed EMBARC, is the largest-ever investigation of psychiatric biomarkers. Biomarkers are physical or chemical characteristics in the body that doctors can measure and analyze as indicators of normal or abnormal biologic processes or responses to a therapeutic intervention.

Co-led by Dr. Fava, EMBARC (Establishing Moderators and Biosignatures of Antidepressant Response for Clinical Care for Depression) is a collaboration with University of Texas Southwestern Medical Center, University of Michigan Depression Center and Columbia University Department of Psychiatry.

“This study represents a giant first step toward personalized medicine for depression,” says Dr. Fava. “The study lays the groundwork for new approaches that will enable a doctor to choose a course of treatment based on data from sources such as a blood test or brain image.”

Another collaborative study led by Dr. Fava (with Yale and Baylor Universities and the National Institute of Mental Health) involves testing the drug Riluzole as an add-on therapy to antidepressants commonly used for people with MDD who do not respond to standard treatments.

Initially approved for the treatment of ALS (Lou Gehrig’s disease), Riluzole has been shown in preliminary research to have a very rapid and long-lasting antidepressant effect. If the study demonstrates Riluzole’s efficacy, it could present a significant breakthrough for approximately 20 million people in the U.S. alone who suffer from treatment-resistant depression.

Ottavio Vitolo, MD, a neuropsychiatrist and clinical researcher in the DCRP, is directing a pilot study on late-life depression (LLD) that uses a sophisticated brain imaging technique, called
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From left, Maurizio Fava, MD, director of the Depression Clinical and Research Program (DCRP) and executive vice chair of the Department of Psychiatry, with Ottavio Vitolo, MD, Albert Yeung, MD, ScD, and Trina Chang, MD, MPH, of the DCRP

Led by program founder and director Maurizio Fava, MD, who also serves as executive vice chair of the Department of Psychiatry, the DCRP has become one of the most highly regarded research, clinical and teaching centers for depression worldwide. In addition to caring for more than 1,000 patients and families each year and training the next generation of clinicians and researchers, the DCRP is consistently credited with conducting some of the most innovative and useful research in the field.

— Treating Major Depressive Disorder

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resting-state functional magnetic resonance imaging, to identify changes in the brain that may show whether a significant subgroup of LLD sufferers with cognitive impairment are more susceptible to developing Alzheimer's disease.

"If we can identify from these early symptoms whether somebody has persistent LLD or dementia associated with Alzheimer's, we can start the appropriate treatment early on," says Dr. Vitolo. "In the future, when more effective medications are available, we may slow down the progression of Alzheimer's disease or even halt it."

ADDRESSING BOTH HALVES OF THE CIRCLE

The evidence for mental health disparities between minorities and non-minorities is clear. In contrast, there are limited data on effective interventions to reduce these disparities. Research studies being conducted by Trina Chang, MD, MPH, and Albert Yeung, MD, PhD, are testing novel interventions to make treatments more effective for underserved minority patients diagnosed with depression.

Dr. Chang, staff psychiatrist in the DCRP, describes MDD as "a vicious circle that can be set off by life problems, and that then causes additional stress by compromising a person's ability to cope with these problems."

Working with adult patients who self-identify as ethnic or racial minorities, her research is testing the feasibility of a stress reduction intervention, added to usual care, for the treatment of depression. The intervention uses a novel combination of relaxation response (RR) training and problem-solving therapy (PST). RR training teaches patients to reduce the effects of stress through techniques such as mindfulness and visualization. PST helps patients understand the connection between their psychological symptoms and their psychosocial problems, and helps them learn to use their own skills and resources to function better.

"By addressing both halves of the circle," notes Dr. Chang, "teaching patients PST for the things they can control, and RR to

cope with the things they can't, we provide them with the skills to break the cycle and prevent relapses when future stresses occur."

BLENDING (MARTIAL) ARTS AND SCIENCE

A growing body of clinical research has begun to evaluate tai chi as a therapy for a variety of health issues. Tai chi is a mind-body exercise that originated in China. Preliminary research has shown its beneficial effects on a range of psychological well-being measures including mood, anxiety, general stress management, self-esteem and quality of life. However, little evidence exists on the effectiveness of tai chi specifically for patients with MDD.

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Trina Chang, MD, MPH

After completing medical training in his native Taiwan, Albert Yeung, MD, ScD, director of Primary Care Research at the DCRP, brought his passion for tai chi to the U.S. When he surveyed the literature, Dr. Yeung found only one published study targeting tai chi for the treatment of depression. The paucity of data inspired Dr. Yeung and his colleagues to conduct a pilot study to evaluate tai chi for treating Asian-Americans with MDD. The initial results were promising.

"We're pleased that the ancient tradition of tai chi may prove surprisingly effective in combating some of modern depression's most debilitating effects," states Dr. Yeung. The team now has a grant from the National Center for Complementary and Alternative Medicine to expand the study.

"We know how depression affects the lives of our patients and their families," says Dr. Fava. "We also know how modestly effective our current treatments are. Our program is committed to leading the way in development of novel and personalized approaches for treating this highly debilitating illness."

Depression Facts

- Major depressive disorder affects approximately 8 percent of American adults every year.
- Depressive disorders are more common among persons with chronic conditions (e.g., obesity, cardiovascular disease, diabetes, asthma, arthritis, and cancer) and among those with unhealthy behaviors (e.g., smoking, physical inactivity, and binge drinking).
- Women experience depression about twice as often as men.
- More than 90 percent of people who die by suicide have a diagnosable mental illness, commonly a depressive disorder.
- Adults age 65 and older die by suicide at a rate higher than the rate in the general population.
- Major depression is the leading cause of disability in the US and developed countries worldwide.
- By the year 2020, depression will be the second most common health problem in the world.