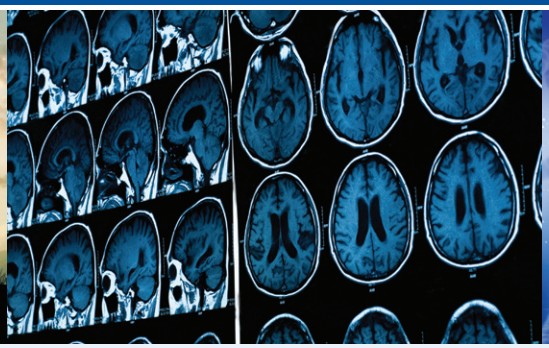
Yale Depression Research Program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Two recent reports by the CDC's National Center for Health Statistics (NCHS) and the U.S. Preventive Services Task Force (USPSTF) have brought the identification and treatment of depression and suicide to center stage.

The NCHS reported that suicide rates increased an alarming 24% from 1999 through 2014. The rates increased for both males and females and for all ages 10–74, with the largest percent increase in suicide rates for females aged 10–14, and for males, aged 45–64.

The USPSTF issued recommendations for regular screening for depression in the general adult population, including pregnant and postpartum women (Siu et al, 2016). The report also stated that the screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up.

The task force found evidence that programs combining these two efforts improve clinical outcomes in adults, including pregnant and postpartum women. Specifically the task force found convincing evidence that treatment with antidepressants, psychotherapy, or both decreases clinical morbidity in adults and older adults with depression identified through screening in primary care settings.

This recommendation has led many institutions and health care practitioners to search for screening instruments that can be implemented with minimal difficulty and cost. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales (PHQ-9) is one instrument that can serve this purpose. The PHQ-9 has reasonably good sensitivity and specificity and can be used to follow patients' response to treatment over time (Kroenke et al, 2010). As with all screening instruments, the PHQ-9 is not sufficient to accurately make a diagnosis of depression, but it is useful in identifying patients who should be considered for further evaluation.

The fact that suicide rates are increasing against the backdrop of a general improvement in the nation's health over the past 10 years again highlights the need for more resources to be made available to identify and treat patients with depression and other mental health disorders. The move to increase screening efforts to identify individuals suffering with depression will hopefully help to stem the disturbing trend of increasing rates of suicide in America.

Anyone interested in participating in research at our clinic, please contact Jane at (203) 764-9131.
Email: depression.research@yale.edu | Visit: depression.yale.edu

New Findings *from the Yale Depression Research Program*

Yale researchers have produced some important findings related to the pathophysiology and treatment of depression over the past few months.

Several papers have been published from both the basic science and clinical laboratories that are begging to shed light on the mechanisms of action that underlie the rapid antidepressant effects of ketamine and other novel agents (Abdallah et al, 2016; Chowdhury et al, 2016; DeLorenzo et al, 2015; Duman et al, 2016). The findings from these studies provide increasing evidence to suggest that drugs such as ketamine, which are able to rapidly increase glutamate synaptic transmission in specific brain regions, lead to changes in synaptic plasticity that appear to be associated with antidepressant-like behavioral effects. By understanding the mechanisms of action related to this novel class of medications, it is possible that we may be better able to understand the pathophysiological mechanisms driving depression and to develop novel treatment strategies.

There have been several new reports examining the clinical efficacy and safety of ketamine treatment. A multisite study sponsored by Janssen pharmaceuticals that included the Yale Depression Research Program demonstrated that both twice and thrice weekly administration of ketamine for up to 4 weeks appeared to be equally effective in terms of meaningful improvement in depression severity (Singh et al, 2016). An analysis of the existing data on ketamine's effects on suicidal behavior was also published (Wilkinson and Sanacora, 2016). The review concluded that although the evidence supporting the clinical use of ketamine for SI is very preliminary, the treatment appears to be a promising therapeutic option in a context where there is a great unmet need, such as in patients at imminent risk of suicide, and calls for further controlled trials to allow for more meaningful clinical recommendations.

Another case report coming out of the Yale-New Haven Hospital interventional psychiatry service presented the first cases in which ketamine was used in the treatment of patients with mood disorders with psychotic features (da Frota Ribeiro et al, 2016). Although the results seemed promising in the two patients receiving the treatment in the controlled setting, it is premature to draw more general conclusions on the safety or efficacy of the treatment in patients with psychotic feature.

The results of another recently completed study examining the clinical efficacy and safety of riluzole in treatment resistant depression was presented at the ASCP meeting last year. The study failed to find any evidence that the adjunctive use of riluzole with standard antidepressant medications was superior to placebo. These results should be available in publication form in the next few months.

A unique pilot study examining the feasibility and potential benefits of using computer assisted CBT to prolong and enhance the response to electroconvulsive therapy was also recently completed. These findings, which suggest future investigation is clearly warranted, should be available in publication form over the next several months. Finally, the results of an important study examining the efficacy and safety of intranasal Esketamine (an enantiomer of ketamine) in the treatment of acute suicidal ideation and behavior should be available within the next several months.

Yale is currently enrolling subjects with depression and other mental health disorders in the following studies: To learn more, visit www.yalestudies.org

Predictors and Mechanisms of Conversion to Psychosis – Dr. Scott Woods | Psychiatry | HIC #0809004203

Multimodal Developmental Neurogenetics of Females with ASD – Dr. Pamela Ventola | Child Study Center | HIC #1206010363

A Phase 2a Study to Evaluate the Kappa Opioid Receptor As a Target for the Treatment of Mood and Anxiety Spectrum Disorders by Evaluation of Whether LY2456302 Engages Key Neural Circuitry Related to the Hedonic Response Trial – Dr. Gerard Sanacora | Psychiatry | HIC #1404013717

Double-Blind, Placebo-Controlled Trial of Ketamine Therapy in Treatment-Resistant Depression (TRD) – Dr. Gerard Sanacora | Psychiatry | HIC#1406014074

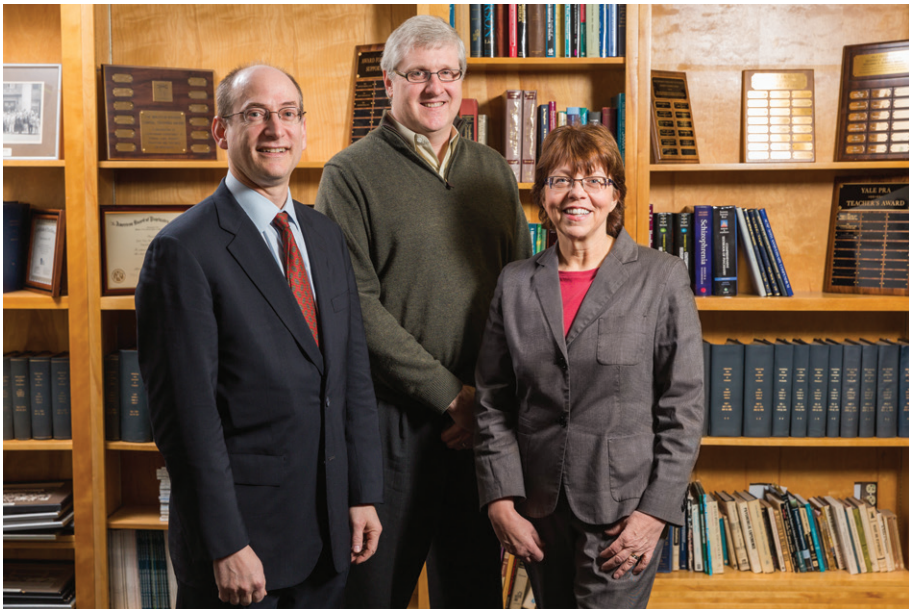
Acetylcholine, Tobacco Smoking, Genes and Nicotinic Receptors – Dr. Kelly Cosgrove | Psychiatry | HIC#1210010989

Biomarkers Development for Mental Disorders – Dr. Chadi Abdallah | Psychiatry | HIC#1501015145

TRANSFORM-3 Intranasal Esketamine Plus an Oral Antidepressant in Elderly Participants – Dr. Gerard Sanacora | Psychiatry | HIC#1510016731

SUSTAIN-2 Intranasal Esketamine in Treatment-resistant Depression – Dr. Gerard Sanacora | Psychiatry | HIC#1601017052

"We see the crippling effects of mental illness and addiction every day. Research is the only way to develop innovative new treatments for these diseases."



Left to right:

John Krystal, MD, *Chair,* Department of Psychiatry
Yale School of Medicine

Robert Malison, MD, *Professor of Psychiatry and Director Clinical Neuroscience Research Unit*
Yale School of Medicine

Stephanie O'Malley, *Professor of Psychiatry and Deputy Chair of Clinical Research*
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Footnotes

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