# Harnessing biology and technology to develop new depression treatments

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New research into the biology of depression, along with new and evolving technologies, provides the basis for developing the next generation of treatments for major depressive disorder (MDD), according to the special January/February issue of *Harvard Review of*

*Psychiatry*.

"By embracing a multifactorial understanding of MDD, by attending carefully to the sex difference in its prevalence and manifestation, and by harnessing new technology, we should be increasingly able to prevent and treat depression," writes Guest Editor Diego A. Pizzagalli, Ph.D., of McLean Hospital, Belmont, Mass.

## Research in Five Key Areas May Point to New Treatments for Depression

Contributed by international experts, the five articles in the special issue provide updates on neuroscience and technology that may inform the development of much-needed treatments for depression. Topics include:

*Gender Differences in Depression*. After age 12, MDD is twice as common in girls compared to boys. Studies have yielded insights into the affective, biological, and cognitive factors contributing to this gender difference—for example, negative emotionality, pubertal hormones, and negative cognitive style. While each factor has a relatively small effect on risk, past and present stressors amplify their impact. Continued research may lead to evidence-based treatments that better take into account the particular needs and circumstances of girls and women.

*Neuroscience and Behavioral Interventions*. "Neuroscience-based augmentation strategies" are being pursued to address two key aspects of depression: anhedonia (loss of interest in pleasurable activities) and cognitive deficits/biases. An approach called Positive Affect Treatment targets issues related to motivation, reward attainment, and reward learning. In an initial clinical trial, this approach showed benefits including decreases in depression symptoms, suicidal thoughts, and stress.

*Role of the Microbiome*. Evidence suggests that the gut microbiome—the community of bacteria and other microbes living in the intestinal tract—may contribute to the development and persistence of MDD. The microbiome is altered in patients with depression, and commonly used antidepressant drugs affect the microbiome. For example, studies have suggested that a diet high in anti-inflammatory foods (such as the Mediterranean diet) may shorten episodes of depression.

*Opioid-Based Therapies*. Compelling evidence suggests that abnormal opioid signaling may play a role in the development of MDD. This may help to explain why many patients don't respond to current antidepressant medications. Opioid mechanisms might also account for rapid antidepressant responses to the anesthetic drug ketamine. Strategies targeting one or more of the four opioid receptor subtypes might open new approaches to treating MDD and other stress-related disorders.

*Technology in Depression Treatment*. Wearable devices, global positioning systems (GPS), and other technologies may provide valuable tools for understanding the wide variation in symptom and disease expression (phenotype) of MDD. For example, GPS devices or fitness trackers may provide useful information on symptoms of social isolation, physical inactivity, and sleep disruption. These and other approaches such as natural language processing and ecological momentary assessment could provide real-time assessment of depression's impact on the lives of individual patients.

While current evidence-based treatments, including antidepressant medications and psychotherapy, are helpful for many people, an "unacceptably high" proportion of patients with depression derive no benefit from these treatments. "There's an acute need for new understandings of depression and its impact on patients' lives," Dr. Pizzagalli comments. "We hope the insights provided by the special issue

papers will help to spur the development of new and better treatment approaches that our patients urgently need."

**More information:** Diego A. Pizzagalli. Introduction, *Harvard Review of Psychiatry* (2020). DOI: 10.1097/HRP.0000000000000244

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