



From Depression to Deep-Learning – Leveraging iPSC and AI Platforms for Evidence-Based Depression Treatment

Psychiatry has spent a century trying to treat what it could not see. Patient-derived neurons are about to change that.

Depression touches a staggering portion of the U.S. population. According to Gallup's 2026 polling,¹ 19.1% of American adults, roughly 51 million people, are currently being treated for depression, and 29.5% report having been diagnosed in their lifetime. Among adults under the age of 30, the rate has more than doubled in less than a decade, climbing from 13% in 2017 to 28% in 2026. The disease accounts for billions of dollars in lost productivity and is consistently ranked as one of the most commonly diagnosed disabilities globally.

Yet, for how common it is, and despite a large market of FDA-approved antidepressants, psychology still hasn't found a reliable way to treat patients quickly. Two-thirds of patients don't respond to their first antidepressant² and even after a few different medication switches, a third of patients still only experience partial relief. Each failed attempt to find the right medication prolongs patients' suffering. A typical antidepressant takes six to twelve weeks to confirm whether it is working, and a patient may cycle through four to six different medications before something fits. With such a long journey towards effective treatment, many patients give up when the extended trial and error and constant side effects don't seem to be letting up. This leads to a substantial share of patients never finding an effective treatment.

Another issue that we encounter more frequently is treatment resistant depression (TRD), defined as an insufficient response to two or more antidepressant medications within a depressive episode or period of sustained depression symptoms. The framing, however, is misleading. These patients are not necessarily resistant to all medications. In many cases, their underlying biology was simply never matched to the right medication type to begin with.

Psychiatry's Missing Biopsy

For decades, every other major branch of medicine has moved decisively toward biology-based decision-making, while psychiatry has been left behind. In oncology, biopsy is the first standard of care. A tumour sample is removed, sequenced, profiled and tested against candidate therapies before treatment begins. Rheumatologists track inflammatory markers. Cardiologists rely on lipid panels, troponin levels and high-resolution imaging. Endocrinologists measure circulating hormones. Across fields, the path from diagnosis to treatment runs through direct biological evidence.

In psychiatry, the prescribing decision has rested almost entirely on indirect inference. A clinician interviews the patient, scores symptoms against a checklist and chooses a medication based on population averages, family history and clinical judgment. The brain itself, the actual organ being treated, has

remained a black box. Even research-grade imaging modalities like fMRI, while increasingly informative at the population level, are not granular enough to predict an individual's response to a drug. The fundamental obstacle has been simple: you can't easily biopsy a living human brain. The tissue is inaccessible and removing neurons in order to test medications against them would do far more harm than the disease itself.

This is true not only for depression but for nearly every major psychiatric and neurological condition. Schizophrenia, bipolar disorder, Alzheimer's and Parkinson's all live in tissue that, until recently, has been impossible to study at the cellular level in individual patients. Psychiatrists have been calibrating against external symptoms or looking at reactions from other organs like the liver, while the underlying biology stayed hidden. It is a gap the field has lived with for so long that, unfortunately, trial-and-error is the standard of care.

What Depression Actually Looks Like in the Brain

The American Psychiatric Association's book, the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), lists nine diagnostic criteria for major depressive disorder, and a patient needs only five of them to qualify. Two patients can therefore carry the same diagnosis with almost no overlap in their symptoms.

Beneath that high-level criteria, however, things get much more complex. In depression, there's generally a reduction in motivation and reward volition, which manifests in the brain as reduced synaptic connectivity or neuronal communication. However, there isn't one sole reason for a change in those network structures. Scientists have found by layering together different types of biological data (genes, how those genes get switched on or off, what they produce and signs of inflammation) that there are four subtypes of depression, each tied to different brain chemicals and their influence on neuronal connectivity. Some are mainly driven by serotonin dysregulation, others by GABA (the brain's primary inhibitory neurotransmitter or "calming" chemical) and others by dopamine and noradrenaline (involved in motivation and reward).

Teen depression looks especially varied. In some teenagers, the brain isn't properly trimming back unused connections between neurons, the way it normally should during adolescence. In others, the inhibitory GABA system isn't doing its job of keeping brain activity in check.

What this means in practice is that depression treatment cannot be a one-size-fits-all. One patient may be facing a serotonin-transport problem while another may have a neuronal plasticity problem. The treatments that can address each of these mechanisms already exist in our pharmacopoeia. The challenge has never been a shortage of drugs. It has been the inability to match a specific patient's biology to the molecule designed to act on it.



Subsection: Neurodegenerative Diseases

To treat depression effectively, clinicians need to understand exactly which neuronal systems are dysregulated in the individual patient. Then they need to be able to check which drugs most effectively engage those systems, changing connectivity and circuit complexity. However, historically, neither of these things could be done without first administering the medication to the patient and waiting.

The iPSC Inflection Point

Luckily, new advances in technology and science are changing this. Induced pluripotent stem cell (iPSC) technology, recognised with the Nobel Prize in Physiology or Medicine in 2012,³ has finally matured to the point where it can be applied clinically. The process starts with a simple blood draw. Those blood cells are then reprogrammed into iPSCs (cells that hold the ability to differentiate into any cell type in the body). From there, those iPSCs are differentiated into frontal cortex neurons. These cells are a very simplified model of the patient's brain, often referred to as a "brain in a dish". They carry the same risk variants, the same expression patterns and the same vulnerabilities that their counterparts in the brain do. This means, for the first time, psychiatry has access to a living, patient-specific sample of the tissue it has been trying to treat.

The implications go well beyond diagnostics. Patient-derived neurons can be exposed to a panel of antidepressants, including SSRIs, SNRIs, atypicals and, increasingly, novel mechanisms such as psychedelic compounds. The cellular response can then be measured directly. The biomarkers that researchers have validated include synaptic connectivity, neuroplasticity, dendritic morphology and gene-expression shifts that distinguish patients who responded to a medication from patients who did not respond. These measurements have been replicated across multiple independent laboratories and are increasingly being treated as legitimate clinical readouts rather than basic science.

The same model is also reshaping psychedelic medicine by using patient-derived neurons from depressed patients to study how drugs like psilocybin restructure synapses in the depressed brain. This is the kind of mechanistic question the field could not previously ask in a controlled environment in research labs. The result is an emerging picture of which patients are most likely to benefit from a psychedelic intervention, which from a traditional SSRI and which may require something else entirely. Following the April 2026 federal executive order accelerating psychedelic research in the United States, work of this kind is moving from the periphery of the field into its centre.

A New Standard of Care Taking Shape

The shift from inference to evidence is the most important change in psychiatric medicine in a generation. Patient-derived neuron platforms will give clinicians an inside look at their patients' brain biology, something previously inaccessible. With this information, they can ground prescription decisions and other judgments in science. Just as oncologists no longer treat breast cancer as a single disease but as a constellation of molecularly defined subtypes, psychiatrists will increasingly treat depression and, in time, schizophrenia, Alzheimer's, bipolar disorder and other psychiatric disorders as cellular phenotypes with predictable drug responses.

The infrastructure is being built now. The Centers for Medicare and Medicaid Services have begun granting clinical

coverage for the first iPSC-derived antidepressant selection tests, a signal that patient-derived neuron diagnostics have moved from a research tool to a reimbursable medicine. Beyond physicians, pharmaceutical developers are also beginning to use these technologies and platforms to stratify trial populations, addressing one of the longest-standing problems in CNS drug development, in which broad patient cohorts have washed out promising compounds for decades.

Depression is one of the most consequential conditions in medicine, and for too long the field has accepted that the path from diagnosis to effective treatment must run through months of guesswork. These new innovations are proving that it doesn't have to. The science has advanced to ground antidepressant selection in a patient's own biology, and both regulatory and reimbursement frameworks are catching up. The clinical evidence is now beginning to follow too. For patients who have struggled for years, this shift in practice could be the catalyst that finally offers relief by addressing the root cause rather than managing symptoms.

REFERENCES

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