



# MAPPING A COMPLEX LANDSCAPE

## *The Promise of Precision Psychiatry and Medical Imaging*

By **Rebecca Montz, EdD, MBA, CNMT, PET, RT(N)(CT), NMTCB RS**

**D**epression is not merely a personal battle; it has evolved into a significant crisis impacting millions, particularly our youth. This widespread mental health disorder can occur independently or alongside other conditions, complicating treatment efforts. Those who have experienced trauma, loss, or high-stress situations are especially vulnerable, with women nearly 50% more likely to suffer from depression than men.

The World Health Organization estimates that 3.8% of the global population is affected, with prevalence rates rising to 5% among adults and 5.7% among those over 60, totaling approximately 280 million people worldwide. Alarming, over 10% of pregnant and postpartum women also experience depression. With suicide being the fourth leading cause of death among 15- to 29-year-olds, the urgency of addressing this issue cannot be overstated.

Treating depression is multifaceted, as each individual experiences it uniquely, with variations in symptoms, severity, and underlying causes. This makes one-size-fits-all solutions largely ineffective.

Treatment options—ranging from cognitive behavioral therapy to antidepressants and lifestyle changes—add complexity to finding the right combination for each person. The search for effective medication often turns into a frustrating trial-and-error process, particularly for those with comorbid conditions such as anxiety or chronic health issues. As a result, personalized approaches are essential for effectively managing this pervasive disorder.

Biological factors, such as brain chemistry and genetics, significantly influence treatment responses, and the understanding of these influences is continually evolving. Additionally, stigma and

socioeconomic barriers often prevent individuals from seeking necessary care. Recent breakthroughs, including the identification of depression subtypes through functional MRI (fMRI), offer promising paths toward more tailored treatment plans. Widespread implementation of these innovative methods is still underway. While the quest for the most effective treatment for depression remains a complex endeavor, these new advancements offer hope for patients suffering from this condition.

### **New Horizons**

Revolutionary research from Stanford Medicine is paving the way for more personalized approaches to mental health treatment. Under the leadership of Leanne Williams, PhD, the first Vincent V.C. Woo Professor of Psychiatry and Behavioral Sciences and director of the Stanford Center for Precision Mental Health and Wellness at Stanford University School of Medicine, a groundbreaking study examined the use of brain imaging to pinpoint distinct subtypes of depression and anxiety. Published in *Nature Medicine* on June 17, 2024, the study categorized



depression into six distinct biological subtypes, or “biotypes,” while pinpointing which treatments were likely to be more or less effective for three of these categories. The collaborative study involved contributions from researchers at institutions including Columbia University; Yale University School of Medicine; the University of California, Los Angeles; UC San Francisco; the University of Sydney; the University of Texas MD Anderson; and the University of Illinois Chicago.

To delve deeper into the biological underpinnings of these conditions, Williams and her team analyzed data from 801 participants diagnosed with depression or anxiety. They employed fMRI technology to monitor brain activity, capturing scans of volunteers at rest and during tasks designed to evaluate cognitive and emotional functioning. By focusing on specific brain regions and their interconnections, the researchers aimed to enhance their understanding of the neural mechanisms driving depression and anxiety.

By employing a statistical technique known as cluster analysis, the researchers identified six distinct patterns of brain activity among the participants. They

subsequently randomized 250 individuals to receive one of three commonly prescribed antidepressants or behavioral talk therapy. The results revealed that patients with a particular subtype characterized by increased activity in cognitive brain regions responded most positively to the antidepressant venlafaxine (Effexor). Conversely, those from another subtype, exhibiting heightened activity in areas associated with problem-solving and emotional regulation during rest, found greater symptom relief through behavioral talk therapy. Furthermore, patients in a third subtype, marked by reduced resting activity in the attention control circuit, were less likely to benefit from talk therapy compared with other biotypes.

The study represented a groundbreaking achievement in the identification of biotypes for more accurate diagnosis and treatment of major depression, utilizing a method that is readily applicable in clinical settings. The fMRI scanning protocols were specifically designed to align with imaging standards used in other medical fields, facilitating their seamless integration into conventional clinical workflows. Ultimately, this approach allows for the

development of customized and effective treatment plans, significantly improving the chances of positive outcomes for those living with depression.

### **Translational Insights**

Williams and her team integrated fMRI to create an innovative method for predicting treatment responses tailored to individual depression biotypes through the analysis of intricate brain activity patterns. The process began with data collection, during which fMRI tracked real-time brain activity, reflecting neural engagement during various tasks or at rest. Researchers categorized individuals into distinct depression biotypes based on these observed patterns, which indicated different underlying mechanisms or symptom profiles.

The incorporation of task-based fMRI significantly amplified the explanatory power of these depression biotypes. Each participant engaged in three straightforward tasks, each lasting five minutes, which were rigorously validated for quality, including optimal signal-to-noise ratios, and designed for compatibility across multiple scanning sites.



Importantly, the interaction of both task-free and task-based fMRI was essential for distinguishing biotypes that respond differently to various pharmacological and behavioral therapies. “Depression is a broad diagnosis that does not inform which treatment would be effective for each patient,” Williams says. “Increasingly, we think of depression as a disorder of brain circuit function. With fMRI, we can directly identify specific disrupted brain circuits in an individual patient, moving beyond the broad diagnosis and tailoring treatment to target the precise circuit affected. Our research indicates the potential of this precision approach to lead to more effective treatment approaches for each patient.”

The research revealed that integrating fMRI circuit measurements with standard clinical assessments substantially improved the predictive capacity for patient outcomes across different antidepressant treatments. Specifically, these findings suggested that such integration could at least double the chances of identifying individuals likely to benefit from treatment. By harnessing fMRI data, it can significantly expand the pool of patients who receive effective interventions, ultimately fostering more personalized and successful therapeutic approaches in the management of depression.

Additionally, the researchers employed a cutting-edge standardized brain scanning technology called the Et Cere Processing System, which quantified circuit dysfunction in each patient by comparing their results against a healthy reference dataset. This innovative approach not only facilitated the selection of patients for upcoming precision psychiatry trials but also allowed for the prospective assignment of treatments customized to meet each individual’s unique needs. Furthermore, this method is particularly well-suited for clinical environments, enabling clinicians to interpret test results with greater efficacy for each patient, as highlighted by Williams.

At Stanford, this advanced imaging technology has been seamlessly integrated into clinical practice through a new precision mental health clinic in collaboration with the radiology department. Similarly, it is being implemented at Gemelli Hospital in Rome, Italy, also in partnership with radiology. This development represents a significant leap forward in enhancing personalized treatment strategies within mental health care, deepening the understanding of

depression, and paving the way for more individualized treatment plans. By leveraging cutting-edge imaging and sophisticated data analytics, health care providers may soon have the ability to tailor interventions based on specific brain activity patterns, resulting in improved treatment outcomes and reducing the often frustrating trial-and-error process that typifies mental health care.

### Essential Discoveries

The key findings of the study revealed significant gaps in psychiatry compared with other medical fields. Currently, psychiatry relies primarily on self-reported symptoms and clinical histories for diagnosis, lacking the integration of biological tests that could improve treatment accuracy. This highlights the urgent need for diagnostic tools grounded in the biological mechanisms underlying these symptoms, paving the way for personalized treatment strategies.

The researchers employed brain scan biotype technology, utilizing fMRI to assess brain activity both at rest and during specific tasks, enabling them to identify dysfunctions within brain circuits linked to depression. Through this approach, Williams and her team discerned a more nuanced understanding of depression and its biological underpinnings. This advancement could lead to more targeted and effective treatment options for individuals grappling with this complex disorder.

Additionally, the team initiated a series of case conferences modeled after tumor boards, focusing on the analysis of fMRI data from their initial patients referred for the Et Cere Processing System. These conferences convene insights from psychiatrists, radiologists, and clinical neuroscientists specializing in neuroimaging, fostering collaborative discussions. A key contributor to this initiative was Eric K. van Staalduinen, DO, clinical assistant professor of radiology at Stanford, whose expertise has been instrumental in guiding these discussions and deepening the understanding of the imaging data.

### Confronting Barriers

The study tackled several methodological challenges in fMRI research, highlighting the urgent need for a standardized approach to data acquisition, preprocessing, and quantification. To address these issues, the team spent years developing the Et Cere Processing System, which comprises three essential components.

First, the system facilitates the execution of imaging sequences and stimulus presentations on both clinical and research scanners using standardized parameters, thereby reducing the workload for MRI technologists. Second, the postscanning phase has been optimized to allow for the quantification of scans in less than one hour, enabling the quick export of scores for each of the six neural circuits evaluated, presented in standardized units relative to healthy reference data. Finally, the system is specifically designed to target neural circuits known to be disrupted in depression and relevant to its treatment.

The research demonstrated the team’s ability to reliably quantify the activity and functional connectivity of these circuits, along with the regions they encompass, in a reproducible manner. The comprehensive approach not only enhanced the reliability of fMRI data but also laid the groundwork for more effective clinical applications in understanding and treating depression. To broaden the applicability of this approach, it was crucial to ensure consistency across various imaging scanners. Achieving clinical translation of these findings required seamless integration with PACS and the quality control protocols employed in clinical settings. Establishing robust connections with these technologies will enhance the reliability and effectiveness of imaging protocols, ultimately paving the way for improved diagnostics and treatment plans across diverse clinical environments.

### Future Directions and Conclusions

One of the team’s primary objectives is to implement fMRI in upcoming prospective biotype trials, where patients will be randomized based on the presence or absence of an fMRI-derived biotype. This groundbreaking approach will allow researchers to compare biotype-specific treatments with standard antidepressant therapies, including selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors. Additionally, the team is engaged in collaborative research aimed at determining how fMRI-derived circuit measurements can predict responses to novel treatments such as psilocybin and how these insights might differ from traditional antidepressant strategies. By pursuing these avenues, the goal is to enhance understanding of treatment efficacy and pave the way for more personalized mental health interventions.

Williams says the research may not have fully captured the extensive range of brain biology associated with this disorder. While the study focused on specific regions implicated in depression and anxiety, there may be other underlying dysfunctions that the imaging techniques did not detect. To delve deeper into these findings, Williams and her team are expanding the study to include a larger participant pool and aim to test a wider array of treatments across all six biotypes, including medications not typically associated with depression management. “Our goal is to find the right treatment for each person the first time, avoiding a long trial-and-error process,” she says. “To do this, we need a deeper understanding of which underlying circuits of the brain are disrupted in each individual person.”

Max Wintermark, MD, chair of the department of neuroradiology at The University of Texas MD Anderson Cancer Center in Houston, says researchers and clinicians are still in the early phases of developing innovative techniques and medications for mental health treatment, highlighting the necessity for further validation of these methods. He says there is a critical need to identify imaging biotypes and biomarker profiles that can accurately predict which patients are most

likely to benefit from these new therapies. Additionally, he notes that depression is one among many mental health disorders, suggesting that similar strategies could be effectively applied to other disorders, as well. He emphasizes that it is important to understand the distinct populations that develop various mental health conditions.

In the clinical setting, Laura Hack, MD, PhD, an assistant professor of psychiatry and behavioral sciences at Stanford Medicine and Teddy Akiki, MD, a clinical scholar of psychiatry and behavioral sciences at Stanford Medicine, have begun to integrate these imaging techniques into their practice through an experimental protocol. Simultaneously, the team is working to establish standardized guidelines for implementing this method, allowing other psychiatrists to adopt these practices effectively. Jun Ma, MD, PhD, the Beth Fowler Vitoux and George Vitoux Distinguished Professor in Geriatrics at University of Illinois College of Medicine, says this is an important advancement: “To truly progress in the field of precision psychiatry, we must identify the treatments most likely to be effective for each patient and initiate those treatments as quickly as possible. Insights into their brain function—particularly the validated signatures assessed in this

study—would greatly enhance our ability to create precise treatment plans and prescriptions for individuals,” she says.

As discussions surrounding the future of mental health treatment progress, van Staaldin says, “This is an exciting time for the practice of medicine, as precision psychiatry unveils a new realm of opportunities for both patients and providers through functional MRI and the quantification of brain circuit dysfunction in major depression. Radiologists must be ready to collaborate with psychiatrists as we advance the field together in this era of personalized medicine.”

Wintermark notes the necessity of an individualized treatment approach that transcends group comparisons, allowing for meaningful feedback through a normative database. He also explains that mental health care is inherently multidisciplinary, with imaging serving a vital role that needs to be contextualized within the patient’s overall health and circumstances.

“A patient is much more than just their imaging results,” Wintermark says. ■

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In addition, powering down one CT unit during nonoperational hours can save 14,000 kWh per year. For some practices, shutting down systems overnight is standard, but for others, it's not. Like other sustainable practices, they vary from hospital to hospital.

Northwell Health in New York has measured and evaluated its own electricity usage with a meter bought on Amazon. The meter was plugged into workstation monitors and power strips. For a month, the baseline energy usage was recorded. The next month, energy usage was recorded after putting monitors to sleep after an hour of activity. Such a project allowed a large facility such as Northwell to evaluate its energy consumption and needs and communicate its findings to the rest of Northwell's departments and hospitals.

At Tisch Hospital-NYU Langone Health, an IR department conducted a life cycle assessment to assess the amount of greenhouse gas emissions in single-use supplies, anesthetics, and the electricity used in procedures over the course of five days. They found that greenhouse gases emitted a carbon dioxide equivalent of 23,500 kg, which is equal to driving a vehicle around 60,000 miles. After further assessment, they discovered the greatest source of emissions came from the energy used to power the HVAC system, 20% to 30% of greenhouse gas emissions came from the HVAC system during off hours. The second greatest source of their emissions came from the production and transportation of single-use surgical supplies.

"The best, most beneficial outcome of the study was that we raised awareness on a topic that very, very few interventional radiologists are thinking about or had been thinking about," says Jonathan Gross, MD, an interventional radiologist at Texas Children's Hospital and Baylor College of Medicine. Texas Children's Hospital, as well as several other IR practices, have created supply packs for different procedures. These packs include the single-use supplies likely needed for specific procedures that the packs target, to reduce the use of unnecessary single-use supplies. With these packs, instead of preparing a set of all supplies available, including supplies not needed or necessary for a procedure, a department can opt to use a pack specifically targeted towards a procedure without the need to open and discard unnecessary supplies.

**"The more we can recognize that the way we practiced in the past is not necessarily going to be the way we practice in the future—if we start thinking about how we want to practice interventional radiology differently in the future, that will continue to keep us in the most cutting-edge position within medicine."**

—Reed Omary, MD, MS, a professor of radiology in the department of radiology at Vanderbilt University Medical Center in Nashville

### Top-Down Initiative

Many in the radiology field feel that a culture shift needs to occur in order for sustainable practices to become the standard. Changes need commitment from leadership down to workers. While climate change and its dangers have been known, the health care system has been slow to make systemic changes. Omary says there are three different ways to make a difference in health care with sustainability: design sustainable medicine with patients, educate and bring awareness to the health care workforce, and provide resources and time for health care to reduce the amount of waste that occurs in the system.

"In addition to our education, we can include sustainability in our guidelines." Gross says. "If there are a range of different studies that we can perform for a particular clinical scenario, let's include sustainability. Certain modalities emit fewer greenhouse gas emissions and contribute less to climate change. Let's prioritize those over CT and MT studies, which we know are far more energy intense than X-ray or ultrasound."

What hospitals and facilities can do is evaluate their own sustainability and develop initiatives based on their assessments. "I would have a direct ask for interventional radiologists, and that is to evaluate the environmental footprint of the products that are used, and where products have similar outcomes and prices, to choose the one with a smaller environmental footprint," Omary says.

A product can be assessed at the beginning of its life cycle based on material selection, manufacturing location, energy source, transport, and labor. Such assessments could include the carbon footprint

of materials used in the manufacturing of the product. Items and questions to think about in terms of sustainability include equipment and supplies. For equipment, things such as imaging equipment or smaller devices such as monitors or blood pressure cuffs. Does the company have an Environmental, Social, and Governance commitment? Are they Energy Star rated, or something similar? Are they made from recycled materials? Do HVAC, lights, screens, and equipment need to be on 24/7? Can you turn them off when not in use or put them on timers or sleep mode? Can you change from fluorescent to LED light bulbs?

For supplies, is the packaging efficient? Can the components, packaging, and drapes be recycled? Excess packaging increases pollution and adds an increase of carbon emissions to the product's volume. Are you using single-use items or items that can be reused? For example, are you providing fabric gowns instead of paper gowns or sending surgical trays back to central sterile instead of using single-use surgical trays? An example of a recycling and reuse project is at the University of Vermont, where the wrappings from sterile items are recycled into plastic bits, then turned into bed pans and emesis basins. Can you create custom packs, and are the items in those packs necessary for the procedure? There are both little and big changes everyone can make if a little more attention is paid to how a lifestyle and practice both at work and at home contribute to a carbon footprint.

### Green Future

Challenges in adopting sustainable practices lie in education, business, and outreach. In the business realm, enthusiasm



needs to be built in order for sustainability to be implemented. “Very often, when speaking with leadership, leading with cost gets their attention. Then, if you could say, ‘It also achieves your goal of carbon neutrality—it’s good for PR’, it’s just like the icing on the cake that can build enthusiasm for projects,” says Drew Caplin, MD, the program director for the integrated and independent interventional radiology residency programs and an associate program director for the diagnostic radiology residency program at the Zucker School of Medicine at Hofstra/Northwell.

A 2023 paper, “Climate Change and Radiology: Impetus for Change and a Toolkit for Action,” proposes radiologists work with vendors to achieve carbon neutrality. Through direct collaboration, radiologists and vendors can create sustainable, user-centered solutions and criteria. Working with vendors can help reduce waste and incorporate sustainable initiatives into practice. Radiologists can also influence vendors to improve sustainability and prioritize energy efficiency. Collaboration with building facilities and design teams can help with waste heat management and recovery by redirecting generated heat from scanner operations.

Additionally, the implementation of AI and remote reporting may reduce unnecessary scanning by leading to higher diagnostic accuracy, shorter examination times, and a reduction in patient travel. Enthusiasm can be built on the peer-to-peer level by implementing rewards for reaching sustainable goals.

For education and outreach, the challenges have one common goal: awareness. “The hurdle we are facing is just the fact that most people aren’t aware of how we are contributing or how our practices are contributing to climate change. But once people are educated, once we talk to people about changing our practices—I think most people are very, very open to that,” Gross says. Despite hurdles towards changes, there is a growing movement to make health care more sustainable. There has been a growing awareness, cited in the increased number of research articles and studies on the topic, as well as a number of radiology societies that have sustainability working groups. Practices can become certified in sustainable health care from the Joint Commission, sign a pledge with the Department of Health and Human Services, and collaborate with the National

Academy of Medicine on sustainable practices within their organization. In fact, more than 100 health care systems have joined the Department of Health and Human Services’ pledge to achieve net zero emissions by 2050.

“The more we can recognize that the way we practiced in the past is not necessarily going to be the way we practice in the future—if we start thinking about how we want to practice interventional radiology differently in the future, that will continue to keep us in the most cutting-edge position within medicine,” Omary says.

Sustainability has a hopeful future in medicine. With many people collaborating on research, ideas, and plans to change practices on individual, local, and global scale. “We recognize that climate change is happening and that it’s affecting all of us and certainly will affect our children and our children’s children’s children. Most people are very concerned and want to do what they can to address climate change and to minimize their impact,” Gross says. ■

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