New Approaches to Improve Schizophrenia Symptoms

New strategies to improve the lives of people with schizophrenia are beginning to emerge, from improved medications to effective cognitive-training programs. “This is a very exciting period in the development of treatments for schizophrenia,” says UCLA psychiatrist Stephen Marder, MD. “There are already some new approaches offering benefits out there, with a very strong possibility of other treatments becoming available very soon.”

Dr. Marder notes that it is important for physicians to recognize that the apathy and lack of motivation and social interest shown by people with schizophrenia is not laziness but part of the illness, and that these new approaches may help them. The same is true for the cognitive deficits, such as impaired attention, memory and decision-making capabilities.
Pediatric Thyroid Nodules
Because thyroid nodules in children are often too small to feel or cause symptoms, children at risk of thyroid cancer should be evaluated at a center with expertise in advanced diagnostic and treatment techniques.

Mental Illness with Co-occurring Addiction
Simultaneous treatment of both mental illness and addiction can increase the chances for long-term recovery from alcoholism or drug addiction.

Reproductive Medicine
Obesity can have adverse effects on fertility, and women should ideally be counseled on the medical, obstetric and neonatal consequences of obesity and its longer-term implications for offspring.

Advances in growing embryos to an advanced stage of physiologic development have made single-embryo transfer a superior procedure for many patients seeking in vitro fertilization.

Geneticists at UCLA counsel patients on the use of prenatal genetic screening, and patients referred for oncology receive therapy that is sensitive to oncologists’ treatment plans.

Pulmonary Medicine
UCLA Peninsula Pulmonary offers comprehensive pulmonary, critical care and sleep medicine services to South Bay residents.

Breast Tomosynthesis
UCLA is among the first medical centers in the region to offer breast tomosynthesis, a new breast imaging technology that improves breast cancer detection rates while reducing false-positive results.

Mindful Awareness
Mindful awareness, a concept focusing on attention and awareness — essentially being “in the moment” — can be a strong antidote for stress, anxiety and depression, and can help alleviate chronic pain.

Pediatric Sports Concussion Clinic
While most young athletes who suffer a concussion will recover with time and rest, some will experience unusual symptoms, delayed recovery or chronic symptoms that can best be treated in a specialized clinic.

Santa Monica Obstetrics and Gynecology
UCLA Obstetrics and Gynecology, Santa Monica combines the comfort and convenience of care delivered close to home with the expertise and technological capabilities featured in major academic medical centers.

Neuroendocrine Tumors
UCLA is the first facility on the West Coast to assess neuroendocrine tumors using DOTATATE PET/CT, which offers image quality that is clearly superior to standard octreotide SPECT imaging.

Severe Mood Dysregulation
New research is under way to determine if severe mood dysregulation should be considered a psychiatric disorder, which could ultimately affect how children with chronic and severe irritability are diagnosed and treated.

To download these and other clinical advances at UCLA Health, go to: uclahealth.org/clinicalupdates

Breast Tomosynthesis
UCLA is among the first medical centers in the region to offer breast tomosynthesis, a new breast imaging technology that improves breast cancer detection rates while reducing false-positive results.

Mindful Awareness
Mindful awareness, a concept focusing on attention and awareness — essentially being “in the moment” — can be a strong antidote for stress, anxiety and depression, and can help alleviate chronic pain.

Pediatric Sports Concussion Clinic
While most young athletes who suffer a concussion will recover with time and rest, some will experience unusual symptoms, delayed recovery or chronic symptoms that can best be treated in a specialized clinic.

Santa Monica Obstetrics and Gynecology
UCLA Obstetrics and Gynecology, Santa Monica combines the comfort and convenience of care delivered close to home with the expertise and technological capabilities featured in major academic medical centers.

Neuroendocrine Tumors
UCLA is the first facility on the West Coast to assess neuroendocrine tumors using DOTATATE PET/CT, which offers image quality that is clearly superior to standard octreotide SPECT imaging.

Severe Mood Dysregulation
New research is under way to determine if severe mood dysregulation should be considered a psychiatric disorder, which could ultimately affect how children with chronic and severe irritability are diagnosed and treated.

To download these and other clinical advances at UCLA Health, go to: uclahealth.org/clinicalupdates
Increased Autism Diagnoses
Indicates Improved Standards for Recognizing Symptoms

Despite the complexities of diagnosing autism spectrum disorders (ASDs), the number of reported cases has increased by more than 20 percent in recent years, an indication that clinicians have become better at recognizing symptoms of ASDs.

“Early identification and intervention are critical,” says Amanda Gulsrud, PhD, clinical director of the Child and Adult Neurodevelopmental (CAN) Clinic at UCLA and a co-investigator in UCLA’s Autism Center of Excellence (ACE). “As we continue to learn more about how to enhance the benefits of behavioral therapies to maximize long-term neurodevelopmental outcomes, we know that one of the most universal and best indicators is the age at which the child enters that intervention.”

Diagnosing ASD in children younger than 3 years of age is often difficult. There is no medical test, such as a blood test, to diagnose ASD. Instead, clinicians rely on behavioral observation and developmental history. The gold standard in the field is the use of the Autism Diagnostic Observation Schedule (ADOS) in conjunction with the Autism Diagnostic Interview-Revised (ADI-R) with the parent or caregiver of the affected child.

From the behavioral standpoint, clinicians look for red flags related to the way a child interacts socially with others, including the use of coordinated eye contact with another person, and the way a child gestures or points when communicating. “We see a wide range of behaviors in children with ASD, and not all treatments will work universally for all children on the spectrum,” Dr. Gulsrud says. “It is important to provide differentiated treatments for children based on their needs and individual symptoms.”

UCLA’s CAN Clinic provides multidisciplinary evaluation and individualized treatment for patients of all ages with suspected or diagnosed neurodevelopmental disorders, with a focus on ASD. Once a course of treatment is prescribed, results should be consistent and measurable, says James McCracken, MD, medical director of the CAN Clinic and director of the Division of Child and Adolescent Psychiatry at the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA.

“Physicians should expect to see concrete evidence of progress in their patients with ASD every three to four months,” Dr. McCracken says. “If not, they should start to ask questions about why the prescribed therapies are not working.”

Dr. McCracken is principal investigator of a $9-million award from the National Institute of Mental Health to create and lead a network of U.S. academic centers that will carry out early “high-risk/high-reward” studies of promising new drugs that may help restore normal development and brain function in children and adults with ASDs.

“Current medical treatments for ASD help to manage difficult behaviors but do not have much impact on the core problems of ASD, despite its known genetic and biological basis,” Dr. McCracken says. “This initiative has the potential to vastly accelerate our progress in this area.”

As part of UCLA’s ACE Center, researchers are also involved in studies focused on a variety of issues related to ASD. They are investigating the genetic and biological underpinnings of ASD, working to improve clinical interventions for 12-to-21-month-old children at-risk for the disorder, using functional magnetic resonance imaging (FMRI) technology to examine infant and child brain development, striving to understand gender differences in symptom presentation and evaluating new treatments for patients with the most severe forms of ASD.

“One-in-three children affected by an ASD never develops the ability to speak in phrases,” says Dr. McCracken. “We are now conducting one of the first studies that tests medication in combination with intensive communication therapy as a way to accelerate uptake of language in these children.”
New strategies to improve the lives of people with schizophrenia are beginning to emerge, from improved medications to effective cognitive-training programs.

Until recently, treatments available for schizophrenia have been dominated by antipsychotic drugs. While such medications reduce the hallucinations and delusions associated with the disorder, they fail to address the major symptoms that impede the daily function of people with schizophrenia — from their school performance to their ability to thrive in the workplace.

The need for medical treatments to improve cognition and negative symptoms for people with schizophrenia led the National Institute of Mental Health to fund a large initiative, Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS), based at UCLA. The initiative is headed by Dr. Marder and Michael Green, PhD. The effort focused on developing better instruments for measuring cognition and negative symptoms in clinical trials, as well as a scientific consensus on the neurobiology underlying these impairments and the most fruitful potential molecular targets for new drug compounds.

Various cognitive-training programs have been designed to help patients improve memory, attention and social recognition.
“Following MATRICS, there has been a huge interest on the part of both the pharmaceutical industry and academia in targeting these domains for schizophrenia for which there have never been effective treatments,” Dr. Marder says. Facilitated by the methods developed in the UCLA-led initiative, a number of promising drugs targeting either the cognitive or negative symptoms have moved into late-stage clinical trials and could be approved by the U.S. Food and Drug Administration sometime in 2014.

At the same time, Dr. Marder notes, there has been substantial activity in the use of various cognitive-training programs designed to help patients improve memory, attention and social cognition. “A number of studies have shown these treatments to be effective,” says Dr. Marder. Effective programs he, Dr. Green and William Horan, PhD, have studied include group-based psychosocial approaches that employ videos and other tools to assist patients in recognizing facial expressions, emotions and gestures.

In the UCLA Aftercare Research Program, an outpatient clinic of the Jane and Terry Semel Institute of Neuroscience and Human Behavior at UCLA directed by Keith Nuechterlein, PhD, which provides diagnosis and treatment services for early-phase schizophrenia patients, faculty have found that Internet-based programs that present a series of challenging mental tasks can, over time, build patients’ cognitive skills in a way that may help them at work and in social interactions.

“The premise of this type of training is based on the plasticity of the brain — its ability to respond to environmental stimulators in a way that can improve neuronal connections and improve the brain’s performance.”

The group led by Drs. Nuechterlein and Ventura has studied the impact of programs that engage participants in computer-based games in which they are challenged to improve on their performance. The researchers conduct a series of cognitive tests both before and after six months of training to determine the extent to which the skills honed in the computer exercises improve overall cognition. The studies have found that participants show a moderate degree of improvement in the cognitive tasks after the six-month training. In addition, study participants showed moderate improvement in their level of engagement in workplace activities. The UCLA researchers are now seeking to determine the optimal level of training for patients, the sustainability of the effects, and how to modify programs to help participants who fail to respond to the training.

“We are very encouraged,” says Dr. Ventura. “We see this type of cognitive training as potentially being one component of a larger package of treatment for people with schizophrenia. It’s not going to replace drug treatment, case management and psychosocial support, but it can be a good complement that, in combination with these other strategies, can significantly improve these patients’ quality of life.”
In the 12 years of conflict in Iraq and Afghanistan since 9/11, tens of thousands of families have experienced a parent being deployed multiple times. Research suggests that such repeated separations amid fears about combat risk increases the likelihood of anxiety and other emotional difficulties in children, as well as contributing to psychological distress in the parent left behind. And the challenges don’t end with the return of the service member, who often struggles to reintegrate while dealing with injuries or significant combat stress reactions.

In 2006, UCLA psychiatrist Patricia Lester, MD, and colleagues at UCLA and Harvard created FOCUS — Families Overcoming Under Stress — to help address the needs of these families. Since then, the UCLA-led program, of which Dr. Lester is director, has touched the lives of more than 400,000 military-family members through evidence-informed resiliency training. Preliminary studies on the effects of FOCUS on military families have found improvements in family communication and functioning, reduced anxiety and depression in adults, and less emotional distress in children.

FOCUS was created to meet the unique psychological health needs of military families facing the prospect of lengthy multiple deployments.

Since its inception, FOCUS has touched the lives of more than 400,000 military-family members through evidence-informed resiliency training. Preliminary studies on the effects of FOCUS on military families have found improvements in family communication and functioning, reduced anxiety and depression in adults, and less emotional distress in children.

FOCUS Attention on Emotional Needs of Military Families

What was the perceived need when you were approached by military mental-health professionals about creating such a program?

The military providers who were seeing these families were facing unique circumstances. For example, parents were unprepared to talk with their children about catastrophic injuries, and it was becoming apparent that the wars we were engaged in were going to mean an extended period of combat with repeated deployments. The psychological-health programming in place at that time was geared more for peacetime circumstances. There was not enough known about how to assist members of military families in coping with separations involving combat, and parents returning with post-traumatic stress and physical injuries. So with feedback from military providers and family members, we adapted resiliency-promoting interventions our group had developed and tested for families facing other types of adversity, customizing FOCUS to the specific circumstances of military families.
Many service members struggle with mental-health problems when they return from combat. What is known about the effects on their spouses and children?

The long-term implications of repeated combat deployments on the psychological health of family members are still being studied, but a growing body of evidence suggests that up to one-third of military children show clinically significant symptoms of anxiety, and that both military children and military spouses have higher rates of referral for inpatient and outpatient mental-health treatment. These long periods of separation in the context of danger are not something you see in a civilian population. For families, this means major milestones in which the parent is not there, and a much greater level of separation anxiety among the children. For spouses who stay home, there is a higher risk of depression, child neglect and maltreatment as they juggle double parenting duties while being worried and distracted about their loved one’s safety. And when the military parent returns coping with mental-health issues, it may be difficult to fully engage in family activities, and some of these behavior changes may be confusing to a child.

What are the key components of the FOCUS program?

We use an approach called indicated prevention — preparing families to better manage the stressful times before there is a clinical need. Over the course of eight weeks, families meet with FOCUS providers. The program starts with an assessment — a resilience “check-in” using Web-based technology to screen for issues known to affect military families — to help tailor the intervention. Through education, families become more aware of the potential impact of deployment on each of them, including the effects of child separation, post-traumatic stress and traumatic brain injury. Family members make a timeline of their experience, documenting their ups and downs in a way that allows them to build on strengths and address stress. They are then taught five resilience skills: emotional regulation, communication, problem solving, goal setting and traumatic-stress-reminder management — learning how to cope with triggers that recall separation, trauma or loss. Often, these families have never really discussed some of the difficult things they’ve been through. Learning honest and effective communication helps them to come together, address misunderstandings and have a clearer sense of their experience, which we know is an important feature of family resilience.

What is known about the efficacy of the program?

We’re in the process of a long-term study of the effects of FOCUS on military families, but preliminary work has found improvements in family communication and functioning. Benefits have included reductions in anxiety and depression in the adults, as well as less emotional distress and fewer problem behaviors in the children and improvements in their peer relationships, pro-social skills and coping.

How has FOCUS been received by the military branches?

FOCUS has been very well received. We have expanded the program so that customized versions are now offered specifically for couples, families with young children and in schools, and for veterans who have returned home to their communities. We are working with UCLA Operation Mend and other partners to deliver FOCUS prevention services through a range of innovative platforms: video teleconferencing, mobile applications and Web-based delivery.

“With feedback from military providers and family members, we adapted resiliency-promoting interventions our group had developed and tested for families facing other types of adversity, customizing FOCUS to the specific circumstances of military families.”
As researchers continue to move toward earlier detection of Alzheimer’s disease through improved neuroimaging strategies and genetic discoveries, a UCLA Alzheimer’s and longevity expert stresses that patients should be advised of the importance of lifestyle in preventing or delaying memory impairment — even if they have yet to show any symptoms.

Although there is no cure for Alzheimer’s, finding ways to detect it at an earlier stage has significant clinical implications, says Gary Small, MD, professor of psychiatry and biobehavioral sciences in the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA and director of the UCLA Longevity Center. “If we can identify problems early, we have a better chance of protecting the brain while there are still intact brain cells,” Dr. Small explains. “It is easier to maintain a healthy brain than to repair a damaged brain.”

Through neuroimaging and genetic studies, researchers are looking for biological markers that will help to detect Alzheimer’s before major damage has occurred. Structural imaging with MRI or CT techniques is routinely used to evaluate patients experiencing memory loss — typically to rule out possible factors such as a tumor or stroke. More revealing in early Alzheimer’s diagnosis is functional imaging with PET scans — in particular fluorodeoxyglucose (FDG) PET, which measures glucose metabolism in areas of the brain that are involved in memory, learning and problem solving.

Now, newer types of PET scans are focusing on the protein deposits that build up in the brain of Alzheimer’s patients as a potential early indicator. This includes an approach developed by Dr. Small and colleagues at UCLA. “We use chemical markers that temporarily attach themselves to the abnormal protein deposits that define the disease: amyloid and tau,” Dr. Small explains. Other approaches attach only to amyloid, he notes, and tau appears to correlate more closely with the disease. Dr. Small’s group is currently studying the approach in research protocols.

What is known about genetic factors falls into two categories. In rare cases, families have an autosomal-dominant inheritance pattern, meaning that half of the family members will get Alzheimer’s disease — typically with early onset. Individuals with such a family history should consult a genetic counselor and potentially be tested for the mutation that is causing the inherited form of the disease, Dr. Small says.

Much more common are genetic indicators that have been found to increase the risk of Alzheimer’s. The best-understood of these is the apolipoprotein E (ApoE) gene, which has three forms: 2, 3 and 4. In the general population, it is estimated that as many as one-in-five people have ApoE4, putting them at a higher risk for Alzheimer’s disease. Because the gene is neither necessary nor sufficient to cause Alzheimer’s, Dr. Small notes, it isn’t recommended as a screening tool. It is, however, useful in research. “If we find that people with mild memory loss who have ApoE4 respond better to a treatment, that is important to know,” he says.
Through neuroimaging and genetic studies, researchers are looking for biological markers that will help to detect Alzheimer’s before major damage has occurred.

But Dr. Small points out that for the majority of the population, nongenetic factors are more important to their brain health — and that lifestyle choices have a much greater impact than most people realize. For example, the widely cited MacArthur study on successful aging concluded that genetics accounts for approximately one-third of cognitive and physical success in aging. “That means two-thirds must be nongenetic,” says Dr. Small, who has written a number of books on the topic, most recently *The Alzheimer’s Prevention Program: Keep Your Brain Healthy for the Rest of Your Life.* “We are learning more and more about these nongenetic protective factors that might be under our control: nutrition, physical fitness, stress management and cognitive exercise.”

In the area of nutrition, perhaps the most important strategy involves weight management. “We know that if you’re overweight, that doubles your risk for Alzheimer’s, and if you’re obese, it quadruples your risk,” Dr. Small says. “The good news is that new studies are showing that if you reduce your weight, you can significantly improve your cognitive performance.” As for what to eat, studies suggest a diet rich in omega-3 fatty acids and low in omega-6 fatty acids is healthier for the brain. Other brain-health strategies include consuming antioxidant fruits and vegetables and minimizing refined sugars and processed foods.

Strong evidence supports the idea that physical fitness — particularly cardiovascular conditioning — can provide cognitive benefits, Dr. Small adds. “During exercise, the heart is pumping nutrients to the brain cells, and the body is producing brain-derived neurotrophic factor, which causes dendrites to sprout branches — the tentacles that connect brain cells,” he explains. Stress management is also believed to be important. Chronic stress in animals, for example, has been shown to lead to memory decline. Human studies have found that people who are prone to stress have higher rates of Alzheimer’s.

Dr. Small and others have also reported findings indicating that mental stimulation, including memory training, improves cognitive performance and may lower the Alzheimer’s risk. Based on that evidence, the UCLA Longevity Center offers memory-related classes in more than a dozen states nationwide, tailored to different populations. Brain Boot Camp, a three-hour course, teaches lifestyle strategies for promoting brain health. Memory Training is a weekly program providing practical techniques for enhancing memory ability over the course of four weeks. Memory Fitness is designed for people in senior living, while Memory Care targets people experiencing mild memory loss and their caregivers.

“There is tremendous interest in these strategies,” Dr. Small concludes. “People want to know what they can do to take care of themselves. As physicians, we should be communicating that information and emphasizing that it’s never too early to start taking proactive steps to protect the brain.”
A major clinical trial has shown that only about one-third of adults with major depression will respond after their first medication trial, and the likelihood that similar therapies will succeed declines with each new attempt, leaving about 20-to-30 percent of patients with treatment-resistant depression (TRD). However, newer neuromodulation therapies, along with refinements in older ones that deliver electrical impulses to specific areas of the brain, can help to restore normal function and improve outcomes.

Mental disorders, including depression, affect an estimated one-in-four adults in the United States each year, and for many patients the first line of treatment is medication. But for those who are unable to tolerate the side effects from prescribed medicines or have tried without success many different drugs, so-called neuromodulation offers the hope of meaningful benefit, says Ian Cook, MD, director of the Depression Research & Clinic Program at UCLA.

“With neuromodulation, we can use noninvasive or minimally invasive techniques to change the levels of activity within targeted circuits of the brain that are important for treating illness, while providing clinically significant benefits, with fewer side effects,” Dr. Cook explains.

One of the newest neuromodulation strategies, trigeminal nerve stimulation (TNS), delivers low-energy electrical stimulation through a patch placed on the forehead to specific areas of the brain associated with epilepsy, depression, attention deficit hyperactivity disorder and post-traumatic stress. TNS was invented at UCLA, by Dr. Cook, neurologist Christopher DeGiorgio, MD, and their colleagues, for treatment of drug-resistant epilepsy, and later has been studied for treatment-resistant depression. Although it is approved in Canada and Europe for those conditions, TNS must still be evaluated in U.S. clinical trials before being considered for FDA-approval. In preliminary studies, TNS has
Neuromodulation Offers Treatment-Resistant Depression New Options for

Researchers are just beginning to understand the stimulation (DBS) is a surgical procedure that parameters and pathways through which TMS with prescribed medicines and therapy. “We still have no clear idea how it all works,” says Alexander Bystritsky, MD, PhD, director of the Anxiety Disorders Program at UCLA. “We need more studies to explore TMS as a stand-alone therapy in patients without prior drug treatments and to investigate how TMS potentially interacts with prescribed medicines and therapy.

Researchers are just beginning to understand the parameters and pathways through which TMS and other neuromodulation strategies may be used for specific psychiatric disorders, according to Dr. Bystritsky. For example, deep-brain stimulation (DBS) is a surgical procedure that involves implanting a pacemaker-like device in the chest wall and placing electrodes in the brain to send out electrical impulses to specific regions of the brain. Although DBS is commonly used to treat the symptoms of Parkinson’s disease and related neurological disorders, severe obsessive-compulsive disorder (OCD) is the only psychiatric condition for which DBS is FDA-approved (under a humanitarian-device exemption). At UCLA, researchers are conducting studies to explore the potential of DBS for treating OCD and depression and other conditions.

The researchers are also exploring noninvasive methods to stimulate deeper structures within the brain, such as deep magnetic brain stimulation (DrTMS) and low-intensity focused ultrasound pulse (LIFUP). Currently Dr. Bystritsky is conducting a study of DrTMS in bipolar disorder. “Bipolar disease is a tricky disorder to treat because antidepressants can trigger patients into a manic state or make them very anxious,” Dr. Bystritsky explains. “A single course of DrTMS combined with mood stabilizers may potentially be effective in quickly treating depression in bipolar patients.” The DrTMS technique was recently approved by the FDA for the treatment of unipolar depression.

In patients with hard-to-treat depression, DBS research is attempting to delineate the dysfunctional brain circuits that are most critical to alleviating depressive symptoms and to determine when DBS is indicated given the inherent risks involved.

“With neuromodulation, we can use noninvasive or minimally invasive techniques to change the levels of activity within targeted circuits of the brain that are important for treating illness, while providing clinically significant benefits, with fewer side effects.”

Newer neuromodulation therapies, along with refinements in older ones that deliver electrical impulses to specific areas of the brain, can help to restore normal function and improve outcomes for patients with treatment-resistant depression. 

“It is hard to find a one-size-fits-all treatment with a condition like depression, so we approach it using different pathways,” Dr. Cook says. TMS is FDA-approved as a stand-alone treatment for depression that is unresponsive to medications, but in practice it is often used as a complementary treatment strategy, added on to medications or psychotherapy.

“Then,” Dr. Espinoza says, “we could avoid much of the suffering patients experience as they go through multiple trials of medications or psychotherapy before getting to the right treatment.”
Resnick Neuropsychiatric Hospital Earns Recognition for Quality Nursing

The Stewart and Lynda Resnick Neuropsychiatric Hospital at UCLA has received the 2013 NDNQI (National Database of Nursing Quality Indicators) Award for Outstanding Nursing Quality in the Psychiatric Hospital Category. The NDNQI Award is presented annually by the American Nurses Association. It recognizes programs that demonstrate excellence in overall performance in nursing quality indicators, based on an annual analysis of NDNQI-participating hospitals.