SPEAKER NOTES

Integrative Approaches to Mental Health

Summarized by Thomas T. Thomas

Dr. Eric Arnold is vice president of Bay Psychiatric Associates and director of ECT and the Inpatient Partial Hospitalization Program at Alta Bates/Summit in Berkeley. Trained in psychopharmacy, psychotherapy, and incorporation of psychodynamic and cognitive behavioral approaches, he uses integrative approaches to mental health such as transcranial magnetic stimulation (TMS), ketamine therapy, and electroconvulsive therapy (ECT), along with psychotherapy, for diverse psychiatric conditions. He spoke about these approaches at NAMI East Bay's Speaker Meeting in March.

Dr. Arnold trained in psychiatry at the University of California, San Francisco before joining Bay Psychiatric Associates. He was also director of the ECT outpatient program at Herrick Hospital in Berkeley for nine years. "I've seen how profoundly helpful these therapies have been for so many people," he said. He also noted that ECT, TMS, and ketamine are often used when psychotropic medications alone are not working.

Medication has its limitations, he said, because it tends to become increasingly less effective over time. This was shown with the STAR*D Trial, the largest trial of antidepressants, which enrolled more than four thousand patients. Reliance on medications alone can thus lead to what is called "treatment refractory depression."

Also, antidepressant medications usually require three to six weeks to begin working and about twelve weeks for a full response. And one in three patients fail to respond. These medications also have a problem with side effects and lack of patient adherence, as well as a high relapse rate. All of the current antidepressants are based on the monoamine neurotransmitters, such as serotonin, norepinephrine, and dopamine.

Integrative psychiatry is a subspecialty, Dr. Arnold said. It generally requires a visit to an office or facility and is based on clinical supervision and monitoring for each treatment. The Food and Drug Administration (FDA) has approved various integrative approaches, including ECT, TMS, vagus nerve stimulation (VNS), deep brain stimulation (DBS), and esketamine (Spravato) treatments (but not the use of ketamine itself yet).

Transcranial magnetic stimulation (TMS) is for moderate to severe depression that is not responding to medication. It can also be used to treat obsessive-compulsive disorder (OCD), smoking cessation, and other off-label conditions. The treatment sends magnetic pulses into the brain over the course of several weeks, and the doctor or technician may use guided imaging to define the area to be stimulated.

People should not apply for TMS if they have metal in their heads, are susceptible to seizures, or have an intracranial mass such as a tumor or an arteriovenous malformation (AVM). The regimen requires the patient having previously been on four medications from two different classes and is not recommended for psychosis or bipolar disorder. TMS is covered by most major insurance plans.

The course of treatment includes an initial setup to find the right spot for stimulation, called the "motor threshold." This is followed by 15- to 20-minute sessions five days a week for seven weeks, or 36 sessions. With TMS there is usually no need for tapering off the treatment or maintenance treatments.

Outcomes, based on a sample of a thousand patients, included 34% remission, 28% recovery, 19% partial response, 14% no response, and 5% withdrawn from treatment. TMS is generally well tolerated, with no need for anesthesia and no post-treatment headaches. Studies have also shown that the responses are "durable."

Ketamine therapy was first used off label in 2007. The medication was originally used as an anesthetic in pediatrics and veterinary care, where a large dose renders the patient unconscious. In smaller doses, it produces a psychedelic experience and general mood improvement. The American Psychological Association (APS) approved consensus guidelines for ketamine treatment in 2018, and Bay Psychiatric Associates began using it in 2017.

We don't understand chemically how ketamine works, Dr. Arnold said. It is believed to block the NMDA receptors for the neurotransmitter glutamate, and it changes the patient's relationship with consciousness.

Ketamine is a minimally invasive treatment that can be administered in several ways, including intravenously by a drip or intramuscularly by injection, and these are faster acting. It can also be administered by a lozenge under the tongue or a nasal spray, and these are slower.

Esketamine, with the brand name Spravato, has been FDA approved for treatment-resistant depression, suicidal ideation or behaviors, bipolar depression, anxiety, post-traumatic stress disorder (PTSD), and OCD. It is contraindicated for patients who are pregnant, have an AVM or brain mass, intercranial pressure, uncontrolled hypertension (high blood pressure), or hyperthyroidism. Because it can cause dissociative and hallucinogenic effects, esketamine should probably be avoided by patients with active psychosis—although it can be used for treatment-resistant psychotic conditions—or with substance abuse issues.

In addition to dissociation, adverse effects can include dizziness, nausea, sedation, vertigo, lethargy, increased blood pressure, and bladder and liver problems.

The course of treatment includes lab work to set a baseline, then an induction course of two times a week for three weeks, a continuation course of once a week for three weeks, then once every two weeks, and finally a maintenance course of monthly or quarterly. Clinical experience supports long-term use of the medication and a high relapse rate after stopping it. The out-of-pocket cost of treatment is about $1,000 to $2,000, and coverage by private insurance varies by carrier.

Electroconvulsive therapy is the gold standard for treatment of depression when other treatments don't work, Dr. Arnold said. Electroshock has been around since the 1930s, when it was associated with treatments like lobotomy and insulin shock. There was a resurgence in the 1980s, after the process was changed and techniques improved.

There is fear around ECT, because the electricity induces a seizure in the brain. But this also releases neurotransmitter chemicals, which have an immediate elevating effect. And then, in the longer term, the seizure creates a neuroplastic reaction, changing how the neurons connect to each other. The treatment works well for refractory depression, bipolar depression, intractable psychosis, personality disorders,

PTSD, and for people who are unable to tolerate medications. ECT also works for people who have tried TMS or ketamine treatments.

"A seizure is not really dangerous," Dr. Arnold said, "because the brain knows how to handle it and suppress the effects." The danger in seizures from a condition like epilepsy comes from the patient falling or biting his or her tongue. ECT can be used by people who are elderly or frail.

There are no absolute contraindications, although it should be avoided by people with intracranial pressure or a brain mass, or who are unable to tolerate anesthetics, or have high a high seizure threshold. Use of ECT is cautioned for people with cardiovascular risks and cognitive impairments—although it can be used by people with dementia.

To begin with, the patient is given a muscle relaxant to paralyze the skeletal muscles, but not the heart or breathing, and an anesthetic to put them to sleep. Then the patient's brain is given ultra-brief pulses of electricity over a period of five to eight seconds, usually on the right side of the brain but sometimes on the left—which side depend on the patient and individual conditions such as handedness. The pulses can also be delivered bilaterally, especially in cases of psychosis. (But the classic case of putting electrodes at each temple is no longer used.)

The standard course is an index course of six to twelve treatments over three weeks, usually on an outpatient basis, and then a continuation course, with the treatments spaced out, rather than stopping, to prevent relapse. Patients can continue taking their medications but should stop taking any anticonvulsants.

The patient usually sees a rapid onset of clinical improvement, generally in two to three weeks or sooner. ECT shows 60% to 90% remission for severe depression and 80% remission of suicidal thoughts. Relapse rates can be up to 50% at one year, but this is lower than with most pharmaceutical treatments alone.

ECT treatment is safe, with instances of adverse effects or death exceedingly low. In Dr. Arnold's experience with ECT, no patient has died, and none has had a heart attack or stroke. Physical side effects can include headache, nausea, and some muscle stiffness or soreness. Cognitive side effects can include retrograde amnesia—inability to form day-to-day memories—which is experienced by about 60% of patients, but these effects are transitory, especially with modern technology and techniques. Some patients report "cognitive clouding" or feeling "spacey," trouble recalling words, and sometimes feeling they are in an unfamiliar space.

Pros and cons vary with each of these integrative treatments.

For TMS, the pros are a high rate of remission, at 60%, no impairment of function, and good acceptance. The con is that it takes time to be effective.

For ketamine therapy, the pros are an effective rate of 70% and rapid onset, and it's generally well tolerated. The cons are durability and unknown long-term safety.

For ECT, the pros are a 70% to 90% effective rate, and it's effective after failing with other integrative treatments. It works for a lot of candidates, and it has a rapid onset in two to three weeks. The cons are that it requires outpatient administration under general anesthetic and has limited durability. Also, patients require some social support, such as being driven to and from appointments, because it's an outpatient treatment requiring anesthesia.

Q. How can a patient access these treatments through the public system and on Medicaid?

A. Access varies by county—Alameda County is good, other Bay Area counties are variable—and requires authorization in the individual case.

Q. Why would you have to try ECT after medication and other treatments have failed?

A. ECT doesn't have to be a last resort. But some patients fear ECT and want to try other means first.

Q. We know that many brain conditions are caused by changes in neurotransmitters. But it seems that TMS and ECT are simply "jolting" the system.

A. The two systems are not the same. TMS stimulates the brain with magnetic pulses, while ECT induces a seizure with different effects—which also includes a release of neurotransmitters.