Environmental and Psychosocial Interventions Help Manage Dementia Behavior

Behavioral disturbances such as apathy, physical or verbal aggression, and agitation are among the most challenging aspects of dementia and are likely to affect most patients at some point in the course of their illness. Immensely distressing to both patients and caregivers, negative behaviors greatly diminish quality of life and often lead to caregiver burnout, early institutionalization and acute hospitalizations.

Instead of psychotropic medications and hospitalizations — which more often harm than benefit patients — care models now emphasize prompt treatment of the organic, psychosocial and environmental factors contributing to challenging behaviors and symptom management using nonpharmacological interventions.

D-BART today
For nearly 20 years, the Mayo Clinic Dementia-Behavioral Assessment and Response Team (D-BART) has been practicing and promoting this patient-centered, multidisciplinary approach, which provides dignity and comfort for people with Alzheimer’s disease and related disorders. For much of that time, neuropsychologist Glenn E. Smith, Ph.D., L.P., and psychiatrist Bruce Sutor, M.D., both of Mayo Clinic’s campus in Rochester, Minnesota, comprised the team.

“The D-BART of today is the modern iteration of a program that began in the early 1990s when we recognized that dementia patients who were referred from long-term care facilities to our psychiatric wards were docile and pleasant when they were with us but exhibited challenging behaviors when they returned to their care facilities. What we realized then is that the problems didn’t reside in the patients but in the setting,” Dr. Smith explains.

Thus began the strategy of meeting patients where they are, literally and metaphorically, including evaluating both dementia symptoms and the psychosocial and environmental context in which they occur.

“About 75 percent of patients in nursing homes have a diagnosis of dementia but nothing more specific, so our first concern is to understand the type and etiology of dementia and to help patients, facilities and families understand that as well,” Dr. Smith says. “Then we try to assess disease severity because we want to help institutions understand the great diversity that occurs in people with dementia. In those with mild cognitive impairment, agitation may reflect boredom and a need for stimulation, whereas people who are lower functioning may be over-stimulated by, say, the noise and congestion of a dining room and need a quieter, more intimate environment.”

Also crucial is a keen understanding of who the person was before cognitive impairment. Dr. Smith cites the example of a former power plant manager who was upsetting fellow diners by touching their plates and silverware. “He once had a very challenging job and was accustomed to being in charge, so we asked him to set out plates and silverware that weren’t actually used and to write out operating procedures for setting the table.”
Ketamine Research Focuses on Mechanisms of Action and Biomarker Development

The most notable limitations of current pharmacological treatments for depressive disorders are low response rates and a long treatment-response time. Recently, the anesthetic drug ketamine, a glutamate N-methyl-D-aspartic acid (NMDA) receptor antagonist, has generated considerable interest because it seems to overcome these limitations. Investigational studies suggest that subanesthesia doses of ketamine can improve mood and suicidal thinking in treatment-resistant patients in a matter of hours.

But Susannah J. Tye, Ph.D., a neurobiologist at Mayo Clinic’s campus in Rochester, Minnesota, says enthusiasm for the drug and its ready availability mean it can be administered without sufficient evidence to guide its use.

“We want to make sure treatment is evidence-based, so we are focusing our preclinical and clinical research on understanding ketamine’s mechanism of action, identifying who is going to respond to it — because not everyone does — and learning how to optimize treatment,” she says. “These are still questions we can’t answer, and we don’t want to implement this novel antidepressant treatment until we can.”

Mechanisms of action

Dr. Tye’s research focuses on understanding the factors contributing to treatment resistance in depression and the neurobiological mechanisms underlying the antidepressant actions of drugs such as ketamine. She notes that alterations in glutamatergic signaling may play an important role in the pathophysiology of depressive disorders and that ketamine might have antidepressant actions by restoring function to this system through two key mechanisms of action.

One is activation of the protein mammalian target of rapamycin (mTOR), which controls protein synthesis critical to cell survival and growth. The other is inhibition of glycogen synthase kinase 3 (GSK3), which has long been implicated in mood regulation and plays an important role in neurogenesis and synaptic plasticity — the regulation of synaptic connections between neurons.
People with a serious and persistent mental illness such as bipolar disorder are more likely to smoke and to have far lower quit rates than the general population. Early estimated prevalence of smoking among patients with bipolar disorder is more than 65 percent compared with 18 percent among the general public, with quit rates, on average, of 16.6 percent and 42.5 percent, respectively.

Compared with bipolar disorder patients who don’t smoke cigarettes, those who are tobacco dependent have higher rates of mixed episodes, suicide attempts, and additional drug and alcohol dependence — all of which contribute to lower response rates to conventional mood-stabilizing treatments.

“Smoking cessation is a critically important piece in designing therapeutic programs for people who have a dual diagnosis of depression and addiction. We must address the fact that when bipolar patients have a smoking problem, their mental illness is more difficult to treat,” says Mark A. Frye, M.D., chair of the Department of Psychiatry and Psychology at Mayo Clinic’s campus in Rochester, Minnesota, and director of the Depression Center there.

So Dr. Frye, in collaboration with smoking cessation clinical researchers Christi A. Patten, Ph.D., a professor of psychology, and Jon O. Ebbert, M.D., from the Nicotine Dependence Center, set out to study the feasibility of using varenicline for patients with bipolar disorder.

Varenicline is an alpha-4-beta-2 nicotinic acetylcholine receptor partial agonist and the first drug to target nicotine receptors. It has proved effective for smoking cessation but is associated with significant psychiatric side effects, including suicidal ideation. In 2014, the Food and Drug Administration reported 34 suicides in the U.S. linked to the drug.

“That’s something we will also look at,” Dr. Tye says, “but based on the work we’ve done preclinically, we believe we can identify not only which patients will respond best to ketamine treatment but how best to treat them with augmentation and maintenance therapies. This is where our biomarker approach has great promise.”

Mayo investigators are also interested in addressing the lack of research on ketamine as a treatment for bipolar depression,” she says. “We have fewer options in patients with bipolar disorder because they don’t respond as well to pharmaceutical interventions and can have an adverse response to some of them. It is critical that research address these issues so we can provide safe and effective treatments for our patients.”

Ultimately, she says, the integration of preclinical and clinical research and the development of biomarkers is “really where the field needs to go.”

For more information
Study design and results
Nine participants were initially enrolled in the 12-week Mayo Clinic study. The mean Fagerstrom Test for Nicotine Dependence score was 7, with a mean 15.8 cigarettes smoked a day, and the mean exhaled breath carbon monoxide (CO) was 20. Treatment adherence by pill count was 90 percent.

Four participants eventually dropped out due to adverse medication effects, unrelated injury and worsening of depressive symptoms, but all showed some reduction in cigarette use and two were not smoking at the time they left the study.

The five participants who completed the study showed a significant reduction in the number of cigarettes smoked a day, urge to smoke and CO levels, though only one achieved abstinence, the primary endpoint.

There was no significant increase in depressive symptoms or suicidal behavior.

Dr. Frye acknowledges the study’s limitations — small sample size and open-label design — but notes that the results suggest that varenicline may help people with bipolar disorder stop smoking with few adverse effects.

Given the high rates of smoking in people with mood and anxiety disorders and potential nicotine withdrawal symptoms, researchers say the study underscores the importance of a comprehensive assessment of mood and anxiety symptoms prior to and during varenicline treatment. A larger study exploring different outcome measures of smoking cessation and mood and anxiety improvement will soon be underway.

For more information