Mayo Provides Integrated Care for People With Gender Dysphoria

Although the true prevalence isn’t known, it is estimated that approximately 1 percent of adults in the U.S. have some degree of gender dysphoria. Only a fraction of them seek medically supervised services, and those who do often encounter significant barriers to care. Mayo Clinic provides education and treatment related to gender dysphoria, including medical and psychosocial interventions to assist in optimizing quality of life for transgender, intersex and gender-nonconforming people.

Cesar A. Gonzalez, Ph.D., L.P., a psychologist who provides collaborative care for sexual- and gender-diverse patients at Mayo’s campus in Rochester, Minnesota, says initial appointments interweave assessment and education in order to provide validation, realistic expectations and, most important, guidance toward congruence between gender identity and expression. The evaluation includes an assessment of a patient’s mental health, quality of life, levels of minority-related stress, capacity to provide consent and understanding of goals. Treatment is highly individualized and reflects diversity of gender identities and expressions.

“Gender transition is less about how people look and more about helping individuals feel congruent with themselves,” Dr. Gonzalez explains. “Some patients don’t undergo surgical interventions; for them, taking hormones may be enough. Others want surgery. It’s about being open to gender fluidity rather than having a stereotyped idea of the gender binary. We don’t want to go from one gender box to another. Instead, we want to help patients find their own authentic sense of identity — a practice that may or may not include medical intervention to facilitate changes in gender expression. Ultimately, it’s all a process.”

For transgender people, the process of confronting cultural expectations of gender expression and how these fit with what is natural for them is intensely complex, challenging and stressful. Many engage in behaviors designed to protect them from the stigma, harassment and discrimination associated with being a minority group, including a lack of spontaneous expression and social engagement. They also face practical challenges, such as deciding which restroom to use, traveling with a passport, and setting expectations with others about preferred names and pronouns.

“Some people will have understood all these issues, but others will not, and that’s why we do an assessment,” Dr. Gonzalez says. “Anticipating issues and building resilience is extremely important.”

Integrated biopsychosocial care model
Mayo providers follow the standards of care established by the World Professional Association for Transgender Health. They also practice a genuinely integrated biopsychosocial model in which various specialists — endocrinologists, psychologists, nurse practitioners, social workers and, eventually, surgeons — play equal roles.

“It’s not just that these highly skilled and compassionate providers are involved; we actually talk to each other and we are fully invested,” says Dr. Gonzalez.
N-acetylaspartate (NAA) is the second most abundant neurometabolite in the human brain. It is localized primarily in neurons where it may serve as an acetate donor for myelin synthesis, maintain brain fluid balance and regulate glutamate (Glu) metabolism. NAA is readily detected by proton magnetic resonance spectroscopy (MRS) and is increasingly used as a marker for mitochondrial activity and neuronal integrity in many disorders, including Alzheimer’s disease.

Paul E. Croarkin, D.O., M.S., and colleagues in the Depression Center at Mayo Clinic’s campus in Rochester, Minnesota, hypothesized that patients with bipolar depression have reduced levels of NAA and that therapy with lamotrigine — an anticonvulsant shown to be neuroprotective against Glu excitotoxicity in cellular and animal models — would increase those levels.

To test their theory, the investigators enrolled 15 patients with bipolar depression and nine healthy controls who were similar in age and sex in an exploratory study. All underwent a baseline 2-D MRS scan, and 10 had a second scan after 12 weeks of open-label treatment with lamotrigine. Five patients dropped out of the study before the second scan.

At baseline, patients with bipolar depression had significantly lower levels of NAA (P = 0.02) and total NAA (P = 0.06) than did the healthy controls. But after 12 weeks of lamotrigine treatment, patients with bipolar depression experienced significant increases in NAA (P = 0.01) and total NAA (P = 0.02). No differences in Glu or Glu plus glutamine levels were seen in either group at baseline, but they were elevated in participants with bipolar disorder post-treatment.

Of the 10 patients with bipolar disorder who completed treatment, five achieved remission with lamotrigine. Dr. Croarkin stresses that no relation was seen between clinical remission and NAA levels, which increased overall.

Nonetheless, this study, which was published in 2015 in *Bipolar Disorders*, is the first to show that lamotrigine can normalize an NAA deficit in bipolar depression. It also corroborates animal and preclinical models of lamotrigine-associated neuroprotection. Dr. Croarkin says two mechanisms of action may be at work: Increased NAA levels might be mediated through activating aspartate N-acetyltransferase, which promotes NAA synthesis, or they may be associated with a reduction in Glu levels. Other studies have demonstrated increased NAA with lithium therapy and glutamate modulators such as riluzole.

Dr. Croarkin acknowledges that the study’s small sample size makes it impossible to determine a relationship between the clinical effects of lamotrigine and changes in NAA. “For our present results, this was a brain change only and did not correlate with symptom improvement,” he says. “We suspect with larger sample sizes a correlation with mood improvement may be evident and so we are pursuing larger studies. MRS measures of NAA are relatively easy to obtain, so perhaps in the future this knowledge could assist clinicians. For example, patients with lower than expected NAA may be better candidates for a drug such as lamotrigine.”

**For more information**
The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) includes revisions to the diagnostic criteria for attention-deficit/hyperactivity disorder (ADHD), one of the most common psychiatric disorders of childhood. The revisions aim to better identify ADHD across the life span by providing specific examples of symptom presentation in children, adolescents and adults and by increasing the age-of-onset criterion from less than 7 to 12 years of age.

The original age of onset, which seems to have been arbitrarily determined, appeared in DSM-III and remained in place for 35 years, although it was not supported by evidence from DSM-IV field trials. The recent change was based on a comprehensive literature review and meta-analysis of evidence regarding age of onset for ADHD and supported by studies showing that most adults report symptoms starting before age 12.

Nevertheless, there is concern that extending the age of onset will increase the already high prevalence of ADHD and lead to the medicalization of normal developmental processes. To examine the clinical validity of increasing the age-of-onset criterion, Jennifer L. Vande Voort, M.D., a psychiatrist at Mayo Clinic’s campus in Rochester, Minnesota, and colleagues at the National Institutes of Health studied the prevalence and clinical correlates of DSM-IV- versus DSM-5-defined ADHD and presentations.

The study focused on 1,894 children and adolescents, ages 12 to 15, drawn from the National Health and Nutrition Examination Survey (NHANES) — a cohort that had aged out of the at-risk period for ADHD as outlined in DSM-5. Parent reports provided information about symptoms, age of onset, impairment, and service and medication use during the 12 months before the study.

12-month prevalence rate increases
The researchers found that expanding the age-of-onset criterion led to an increase in the 12-month prevalence rate of ADHD from 7.38 to 10.84 percent. The greatest increase occurred for the inattentive presentation, confirming findings from earlier studies that children with inattentive symptoms have a later age of onset than those with primarily hyperactive symptoms do.

“Children with the inattentive subtype often go unrecognized until later on, when schoolwork gets more challenging,” Dr. Vande Voort says. “Unlike hyperactive kids, they’re not disruptive in class, so they tend to be diagnosed later. By then, they’re already falling behind academically.”

One of the most noteworthy findings is that children whose onset was between the ages of 7 and 12 years were more likely to come from lower income and ethnic minority families. This may result from a lack of access to health care or failure to understand ADHD symptoms and treatments. By the time some of these children see a doctor, they may be overlooked because they’re beyond the age 7 cutoff,” explains Dr. Vande Voort.

Although the study has limitations, she says the findings support expanding the age-of-onset criterion. “Nearly 3.5 percent of kids who have ADHD symptoms would not have been recognized simply because of their age,” she says. “Our study showed that the severity of symptoms is the same in the early-onset and late-onset groups. These symptoms are impairing academic and social development and need to be addressed and treated. My hope is that through our study, we will get the word out to psychiatrists and pediatricians that the diagnostic criterion for ADHD has expanded from 7 to 12 years of age, and that this change can make a difference in children’s lives.”


For more information
In the News

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Dr. Croarkin is focused on understanding the neurobiology, optimal treatment and classification of mood disorders in children and adolescents. Dr. Frye has a research focus on genomics, brain imaging and neuroendocrinology of mood disorders and alcoholism.

Education Opportunities

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Psychiatry Clinical Reviews 2015
Oct. 15-17, 2015, in Chicago

This course provides clinically relevant updates for managing psychiatric problems across all care settings. Topics include mood, anxiety and psychotic disorders; child and adolescent psychiatric treatment; psychotherapy techniques and strategies; sleep disorders; and a neurology update.

Translational Review of Mood Disorders and Addiction 2015
Oct. 29-31, 2015, in Minneapolis

Mood and addiction disorders are two of the most prevalent psychiatric conditions, with a high rate of illness morbidity and comorbidity. This course provides a wide-ranging overview of basic, translational and clinical research in both mood and addiction.

International Dementia with Lewy Bodies Conference 2015
Dec. 1-4, 2015, in Fort Lauderdale, Fla.

Lewy body dementia is the second most common type of dementia. An international group of experts provides updates on key neuropsychiatric aspects of the disorder as well as genetics, biofluid correlates, molecular biology, current symptomatic therapies and future potential disease-modifying treatments.

Depression and Bipolar Disorder on Stage: Science of Healing and Stories of Hope
May 5-6, 2016, in Minneapolis

This innovative program addresses issues associated with the stigma of psychiatric illness and improves participants’ understanding of the cost and challenges associated with depression and mania through insights provided by faculty and audience interactive participation.

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