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Victoria Hendrick, MD
Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Gender-Affirming Care

Learning Objectives

After reading these articles, you should be able to:

1. Diagnose and manage depression and neurocognitive impairment in patients with HIV.
2. Utilize various gender-affirming care treatment options.
3. Identify psychiatric contraindications for transplant recipients or donors.
4. Differentiate between PNES and epileptic seizures.

Management of Depression and Neurocognitive Impairment in Patients With HIV

Garrett Rossi, MD. Inpatient/consult attending psychiatrist, AtlantiCare Regional Medical Center. Pomona, NJ.

Dr. Rossi has no financial relationships with companies related to this material.

Human immunodeficiency virus (HIV) is a retrovirus that causes not only progressive immunologic disease but also neurologic disease. With the advent of effective highly active antiretroviral therapy (HAART), HIV has become a chronic, treatable illness. However, many patients experience mood and cognitive changes, especially if their HIV is poorly controlled. In this article, I will review approaches for the evaluation and management of depression and neurocognitive impairment in patients with HIV.

Depression in HIV-infected individuals

Individuals with HIV/AIDS have more than double the risk for depression

Highlights From This Issue

Lead article
We discuss evaluation and treatment strategies to help address mood and cognitive changes in patients with HIV.

Lead Q&A
How can we best provide gender-affirming care to our transgender and gender-nonconforming patients? Dr. Hansel Arroyo shares key insights and provides a helpful glossary of gender-affirming terminology.

Q&A on page 7
The number of patients receiving organ transplants grows every year. Dr. Paula Zimbrean reviews special considerations in the psychiatric treatment of these patients.

Article on page 9
Your patient falls on the ground and experiences a tonic-clonic seizure. Or does she? We'll help you distinguish between epileptic and psychogenic nonepileptic seizures.

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Q&A With the Expert

Understanding Gender-Affirming Care
Hansel Arroyo, MD

Assistant professor of psychiatry, Icahn School of Medicine at Mount Sinai. New York, NY.

Dr. Arroyo has no financial relationships with companies related to this material.

CHPR: Dr. Arroyo, please tell us about yourself and your background.
Dr. Arroyo: After residency, I completed a consultation-liaison fellowship where I specialized in HIV psychiatry and worked mostly with LGBT patients. For the last six years, I have been director for the Center for Transgender Medicine and Surgery at Mount Sinai, where most of our patients are either trans, genderqueer, or gender expansive.
CHPR: Can you review the meanings of gender expansive, genderqueer, and any other terms relevant to this patient population?
Dr. Arroyo: Sure. The language is constantly changing. "Transgender" refers to an incongruence between the person's sex recorded at

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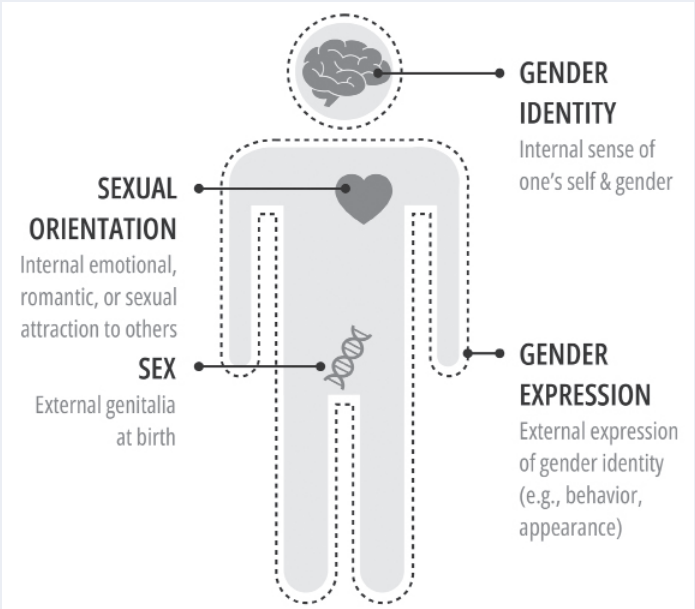
birth and their gender. The term "cisgender" means that the person's sex recorded at birth and gender are aligned. Terms like "gender nonbinary" and "gender nonconforming" imply that the individual doesn't subscribe to the binary polarization of masculine/feminine. "Gender expansive" is a newer and more inclusive term. "Genderqueer" is another relatively new term. A person who says they're genderqueer is saying, "I don't subscribe to the binary." Queerness can also be used to describe sexual attraction—whom a person is attracted to physically, spiritually, and emotionally—and includes gay, lesbian, bisexual, pansexual, and asexual individuals.

CHPR: Have there been any other changes in the terminology of late?

Dr. Arroyo: A recent change is "sex recorded at birth" versus "sex assigned at birth." We make a distinction that the sex at birth is simply what's recorded by the physician after examining the baby's genitalia, but it's not the "assigned" sex as that may change based on how children identify or view themselves as they get older. Another important term is "gender expression," which is how one chooses to express their gender. This may or may not be congruent with either their sex recorded at birth or their gender identity *(Editor's note: See "Understanding Sexuality and Gender" figure)*. For example, you may identify as female, but want to express yourself in more of a masculine way. Some trans women express masculine qualities while other trans women express more feminine qualities. It's important to practice not putting individuals into our own preconceived boxes.

Understanding Sexuality and Gender



Graphic created by Adrienne Grzenda, MD, PhD

CHPR: Can you give us an overview of the mental health needs of transgender and gender-nonconforming patients?

Dr. Arroyo: Sure. The US Transgender Survey showed that trans patients have higher rates of self-reported psychological distress and less access to mental health services. The National Center for Transgender Equality released this report in 2015 and it's the largest survey of trans people's experiences in the US, including their physical and mental health needs (www.tinyurl.com/3cvxjwa6). Several studies have shown that this population experiences higher rates of depression, anxiety, and substance use disorders compared with the general population (Dhejne C et al, *Int Rev Psychiatry* 2016;28(1):44–57).

CHPR: Is treating transgender patients different from treating other patients who suffer from depression and anxiety?

Dr. Arroyo: Treating transgender patients with depression or anxiety is not inherently different from treating other patients, but the mental health provider must have literacy and competency in the needs specific to transgender people. For example, transgender patients are more likely to have struggled with discrimination, rejection, or abuse. Thus, to better frame the treatment plan, the provider should be familiar with caring for patients with trauma and minority stress, and they should be familiar with issues of intersectionality. This last point requires an understanding that each person's experiences of discrimination are unique and involve overlapping categorizations including race, gender, and social class.

CHPR: Can you explain the meaning of the term "gender-affirming care"?

Dr. Arroyo: Gender-affirming care refers to a philosophy of care that respects a patient's gender identity and doesn't impose a "one size fits all" approach. Gender-affirming treatments come in many forms, and no one trans experience is universal. Some trans people transition socially, while others choose to transition chemically or surgically. But not every trans person sees themselves

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This CME/CE activity is intended for psychiatrists, psychiatric nurses, psychologists, and other health care professionals with an interest in the diagnosis and treatment of psychiatric disorders.

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in a binary way, needing to be surgically feminine or surgically masculine. In all cases, it's important to provide patient-centered gender-affirming care.

CHPR: Can you tell us about the types of gender-affirming treatments?

Dr. Arroyo: Sure. There are two main treatments: hormone replacement therapy (HRT) and surgery. HRT decreases depression, anxiety, and PTSD; the only symptom that HRT doesn't quite help is self-perceptions of one's body (White Hughto JM et al, *Transgend Health* 2016;1(1):21–31). This makes sense—while hormones change patients phenotypically, there are limitations to the degree of physical change, so often people will opt for surgical interventions. I should point out, though, that the data come from uncontrolled cohort studies. The studies behind surgeries show a decrease in gender dysphoria and a high rate of satisfaction: around 95%–100% satisfaction from surgical outcomes (van de Grift TC et al, *J Sex Marital Ther* 2018;44(2):138–148). Recent studies have also reported an association between gender-affirming surgeries and improved mental health outcomes (Almazan AN and Keuroghlian AS, *JAMA Surg* 2021;156(7):611–618). And research in veterans has found that the combination of HRT plus both chest and genital surgery results in lower rates of suicidality when compared to no intervention, HRT alone, or HRT plus only chest or genital surgery (Tucker RP et al, *Psychol Med* 2018;48(14):2329–2336).

CHPR: How do mental health outcomes compare following HRT vs surgical interventions?

Dr. Arroyo: It's hard to compare surgical interventions with hormonal treatments because in the US, insurance requires that patients be psychiatrically cleared before surgery. For example, in our clinic we don't clear patients for surgery if they have active symptoms of depression. Since everybody who has surgery has already been deemed to be psychiatrically stable, it's hard to measure a before and after effect of the surgery.

CHPR: But a patient's depression might be related to their gender dysphoria, right? Yet they can't get the surgery that will help address the gender dysphoria because of their depression.

Dr. Arroyo: Right, so it's important to try to distinguish depression due to those reasons vs an endogenous major depressive episode. But ultimately, the important thing is the patient's well-being. The fields of transplant and bariatric surgery follow a similar practice where patients are psychiatrically cleared prior to surgery, as this improves surgical outcomes. For example, a clinically depressed patient might fail to attend postop appointments or practice proper wound care.

CHPR: Are there other measures besides mood that can be used to compare mental health outcomes following HRT vs surgery?

Dr. Arroyo: We also look at body satisfaction or decrease in gender dysphoria, and these measures show that the interventions result in comparable mental health outcomes (van de Grift TC et al, *Psychosom Med* 2017;79(7):815–823).

CHPR: How available are gender-affirming treatments?

Dr. Arroyo: They are now widely available for those who are insured. In 2014, Medicare reversed the ban on transgender services. Most insurance policies cover HRT, and at least some surgical interventions, like chest feminization or masculinization surgery, and "bottom surgeries" or genital surgeries including vaginoplasty, orchiectomy, metoidioplasty, and phalloplasty, are considered medically necessary *(Editor's note: See "Common Gender-Affirming Terminology" table)*. Over the last few years, we've also seen increases in coverage for facial feminization and masculinization surgeries, which historically were considered only cosmetic. Other surgeries like body contouring aren't covered by insurance yet. Some insurers will cover electrolysis or laser hair removal *Continued on page 4*

"Treating transgender patients with depression or anxiety is not inherently different from treating other patients, but the mental health provider must have competency in the needs specific to transgender people. To better frame the treatment plan, they should be familiar with caring for patients with trauma and minority stress."

Hansel Arroyo, MD

Common Gender-Affirming Terminology

Term	Definition
Body contouring	Medical or surgical interventions to reshape areas of the body, like hips or buttocks
Facial feminization surgery	Surgery or procedures to create a feminine appearance to the face
Feminizing mammoplasty	Breast augmentation
Metoidioplasty	Female-to-male sex reassignment surgery
Nonbinary, genderqueer	Not subscribing to a binary (male-female) system
Orchiectomy	Surgical procedure to remove one or both testicles
Phalloplasty	Surgical procedure to construct or reconstruct a penis
Subcutaneous mastectomy	Masculinizing chest reconstruction
Transgender	Sex recorded at birth and gender identity are not aligned ("on the other side")
Vaginoplasty	Surgical procedure to create a vagina

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on the face or genital area, or Botox and fillers, but many don't.

CHPR: When trans patients are admitted to psych inpatient units and they're on hormonal treatments, some clinicians can be hesitant about continuing these hormones since they're not used to prescribing them. Are there adverse consequences to suddenly stopping these supplemental hormones?

Dr. Arroyo: That's a common consultation question from emergency departments and inpatient units, where the doctors ask, "Do we continue the hormone treatment?" And the answer is "yes," unless there's a medical concern, like the risk of coagulation for someone on estrogen. Historically, it was believed that testosterone for trans men caused manic-like symptoms. Those concerns came from the bodybuilding literature where the testosterone levels were supratherapeutic. In those patients, you can see irritability, mood lability, anger, and agitation that might resemble a manic episode. But for trans patients, testosterone levels are usually monitored to be within the normal ranges of their cis counterparts, so there is no need to worry that manic-like symptoms are the result of the hormones. My recommendation is to check the patient's testosterone levels and make sure that they are within the appropriate age range for their cisgender counterparts. Stopping testosterone abruptly can result in increased gender dysphoria and can create low energy, low mood, irritability, and low libido.

CHPR: What about estrogen?

Dr. Arroyo: The two main feminizing medications are estrogen and spironolactone. For trans women, their estrogen levels should be within the normal range, compared to their cis female counterparts of the same age. In general, you don't have to worry that estrogen will cause mood instability. On the contrary, often we see patients who are depressed, and their primary care provider sends them to us asking, "Can you start her on an SSRI?" We evaluate them and we often instead recommend starting HRT first. You'd be surprised how often the mood symptoms lift, partly because they were so interconnected with the gender dysphoria. And if you stop the hormonal medication on the inpatient unit, the patient might then have a relapse of or an increase in depressive symptoms.

CHPR: What hormone levels do you measure, specifically?

Dr. Arroyo: We check total and free testosterone. Depending on age, normal testosterone levels range from 200–1000 ng/dL, and free testosterone levels range from 40–245 pg/mL. For estrogen, we measure estradiol, and normal levels range from 30–400 pg/mL for premenopausal women and 0–30 pg/mL for postmenopausal women. These ranges are based on cis individuals. We use cis counterparts to determine the appropriate ranges for trans people, although there is quite a bit of debate on the appropriateness of doing so.

CHPR: Are there any side effects we should watch for when patients are on hormonal supplements?

Dr. Arroyo: Primarily, the concern is for thromboembolic events in patients on estrogen, especially for patients who smoke as they are at higher risk. Two- to four-fold increases in myocardial infarction have been documented in transgender men, although there are probably many reasons for this higher rate besides hormone exposure, like social stressors and health disparities (Alzahrani T et al, *Circ Cardiovasc Qual Outcomes* 2019;12(4):e005597).

CHPR: Do you have any concerns that the hormones will interact with the patient's medications?

Dr. Arroyo: Only with certain medications. If somebody is on spironolactone and you start lithium, you must closely monitor the lithium levels because spironolactone reduces the renal clearance of lithium and can lead to lithium toxicity. Carbamazepine and oxcarbazepine can reduce estrogen levels, so if a trans woman is on these medications, you must monitor the estrogen levels. With divalproex (Depakote), you need to be mindful of polycystic ovary syndrome (PCOS) in trans men whose ovaries and reproductive system are intact. Also, divalproex-induced alopecia may produce psychological consequences if the individual is already experiencing testosterone-induced hair loss.

CHPR: Are there any other hormonal issues we should consider?

Dr. Arroyo: It's important to monitor for antipsychotic-induced hyperprolactinemia, especially in trans men. If they start developing breast tissue or milky nipple discharge, those side effects can exacerbate gender dysphoria *(Editor's note: See* CHPR *Jul/Aug/Sept 2021 for more on antipsychotic-induced hyperprolactinemia)*.

CHPR: When a trans person is admitted to an inpatient unit, how do you make decisions about what room to place them into? I've encountered situations where a trans patient wants to be in a room with cis counterparts, but we've had some concerns—for example, a trans man who retains prominent feminine features is at risk of being sexually harassed in a room with cis men.

Dr. Arroyo: First we ask about the patient's preferences and see if we can accommodate them. If a patient wants a single room, we try to accommodate that request. On the medical side, it's easier to give them a private room. In our psychiatry unit, we have some two-patient rooms that we can convert into a single room. I had a case involving an incarcerated trans man who wanted to be with other cis men. In the prison system, we thought that would be unwise as the patient would be at risk of being assaulted. We wanted to honor the patient's request, but we did not feel comfortable putting them at that risk. In the inpatient setting, the risk of assault or violence is not that extreme, but you still need to take potential risks into account and have a dialogue with the patient about the options and risks.

CHPR: So, it's best to make these decisions on a case-by-case basis, trying to accommodate patients' wishes as much as possible while keeping safety issues in mind.

Dr. Arroyo: Right.

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Expert Interview – Understanding Gender-Affirming Care

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CHPR: Have you seen a greater openness among clinicians with regard to accepting gender-nonconforming patients?

Dr. Arroyo: My sense is that yes, there's greater acceptance, but we don't have a lot of data on that question. However, we have made clear progress in terms of more individuals feeling comfortable identifying as genderqueer, gender expansive, and trans. The more society learns about gender and gender expression, the less people will be bound to the traditional male/female binary. More adolescents are identifying as genderqueer or gender expansive and leaving the binary terms of male/female behind. And whether they are trans or not, they are increasingly turning away from the idea of being anchored by those two poles.

CHPR: Thank you for your time, Dr. Arroyo.

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Management of Depression and Neurocognitive Impairment in Patients With HIV

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compared to the general population, occurring in roughly 30% of patients (Rezaei S et al, *BMJ Support Palliat Care* 2019;9(4):404–412). Distress from the HIV diagnosis, loss of loved ones to HIV, stigma associated with the virus, HAART side effects, and direct effects of the virus on the brain can all contribute to this high rate.

Assessment

Some depressive-like symptoms—eg, fatigue and poor concentration—might represent medication side effects and HIV-related complications, like HIV-associated neurocognitive disorders. How can we determine whether a patient's symptoms are due to an underlying depressive disorder? If a patient's HIV infection is well controlled and their viral load is undetectable, I treat any depressive symptoms as primary depression. In patients with more advanced infections or poor compliance with treatment, lethargy and cognitive impairment may be secondary to the HIV infection rather than depression. Screening for anhedonia, hopelessness, and suicidality will help in reaching the right diagnosis.

HIV-infected patients are at high risk for suicide, particularly in the days immediately after their HIV diagnosis. Suicide risk correlates most strongly with the development of depression, but several other factors add to this risk, including substance use, personality disorders, and disease progression. The use of certain antiretroviral drugs also increases the risk of depression and suicidality (see "Neuropsychiatric Side Effects Associated With Medications Used in HIV/AIDS" table). It's important to perform suicide screenings for all patients with HIV, ideally with validated screening instruments such as the Columbia-Suicide Severity Rating Scale (C-SSRS).

My evaluation focuses on the identification of psychosocial stressors, medication changes, substance use, and the progression of the patient's HIV infection. I generally obtain hepatic and thyroid function tests, HIV viral loads, CD4 counts, tests of gonadal function (testosterone and dehydroepiandrosterone), and hematological function (hemoglobin, hematocrit, and serum erythropoietin). Why do I obtain these tests? Most psychiatric medications are metabolized by the liver, and HIV infection is often comorbid with hepatitis C and other liver infections, thus a liver function panel can alert us to any hepatic dysfunction. Hypothyroidism is a potential cause of depressive symptoms and should be screened for in this population. CD4 counts and viral loads help assess for compliance with HAART and are a marker for disease progression. Hypogonadism and low testosterone levels are common in HIV-infected men and may produce lethargy and low libido. Testosterone replacement can be considered in severe cases. Anemia can be a source of fatigue, so hemoglobin/hematocrit levels help in the workup of low energy in patients with HIV (see "Lab Testing for Patients With HIV and Psychiatric Symptoms" table).

Some clinicians use screening scales like the Beck Depression Inventory

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Neuropsychiatric Side Effects Associated With Medications Used in HIV/AIDS

Medication	Side Effects
Acyclovir	• Agitation • Confusion • Depersonalization • Visual/auditory hallucinations
Corticosteroids	• Confusion • Depression • Mania • Psychosis
Efavirenz	• Anxiety • Confusion • Depression • Nightmares • Sleep disturbances
Zidovudine (AZT)	• Agitation • Confusion • Insomnia • Mania at high doses

Lab Testing for Patients With HIV and Psychiatric Symptoms

Tests	Rationale
CD4 counts	This information helps assess for compliance with HAART and is a marker for disease progression
Gonadal function (testosterone, dehydroepiandrosterone)	Hypogonadism and low testosterone levels are common in HIV-infected men and may produce lethargy and low libido
Hematological function (hematocrit, hemoglobin, serum erythropoietin)	Anemia can be a source of fatigue
Hepatic function	Most psychiatric medications are metabolized by the liver, and HIV infection is often comorbid with hepatitis C and other liver infections
HIV viral loads	This information helps assess for compliance with HAART and is a marker for disease progression
Thyroid function	Hypothyroidism is a potential cause of depressive symptoms

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(BDI), but HIV-associated somatic symptoms (eg, fatigue, loss of appetite) might inflate the scales' scores, potentially causing patients to seem more depressed than they are. The Hospital Anxiety and Depression Scale (HADS) is a validated instrument for detecting depression and anxiety in the hospital or outpatient clinic. HADS scores were found in one study to be unconfounded by the presence of HIV symptomatology and may represent the most reliable and valid screening method for depression and anxiety in HIV patients (Savard J et al, *J Pers Assess* 1998;71(3):349–367).

Drug Interactions Associated With HAART

Medication	CYP450 Interactions	Potential Psychotropic Interactions
Cobicistat	CYP3A4 inhibitor	Increased concentrations of alprazolam, aripiprazole, quetiapine, triazolam
Efavirenz and etravirine	CYP2C19 inhibitors	Caution with citalopram above 20 mg
Lopinavir	CYP2B6 inducer	Decreased bupropion concentration
Nevirapine	CYP3A4 and 2B6 inducer	Decreased bupropion concentration
Ritonavir	CYP2D6 and 3A4 inhibitor, CYP2C19 and 1A2 inducer	• Increased concentrations of duloxetine, fluoxetine, trazodone, tricyclic antidepressants, aripiprazole, alprazolam, triazolam, quetiapine, lurasidone • Decreased concentrations of escitalopram/citalopram, sertraline, clozapine, and olanzapine levels

Treatment

Psychotherapy and selective serotonin reuptake inhibitors (SSRIs) are first-line therapies for the treatment of depression and anxiety in patients with HIV. Tricyclic antidepressants, which slow gastrointestinal motility and promote weight gain, may be particularly good options for patients with diarrhea and wasting. However, tricyclics are highly anticholinergic and can produce or exacerbate cognitive impairment. Mirtazapine is another option as it stimulates appetite without producing anticholinergic side effects. Bupropion is helpful in cases where fatigue and impaired concentration are primary symptoms, but its dose-dependent seizure risk complicates treatment in patients with neurologic complications from HIV (eg, cerebral toxoplasmosis). I sometimes use psychostimulants, including modafinil, methylphenidate, and dextroamphetamine, as adjunctive treatments for fatigue and apathy when these are refractory to other treatment options.

Hypotension is a frequent complication of advanced HIV disease, so I minimize the use of medications that lower blood pressure (eg, prazosin and clonidine). I rarely use ECT for HIV-infected patients due to its risk of cognitive dysfunction, including anterograde and retrograde memory loss. When I prescribe antidepressants to patients on HAART, I try to be mindful of drug interactions (see "Drug Interactions Associated With HAART" table).

I urge patients to join support groups, as group psychotherapy not only improves depressive symptoms but also enhances social supports, coping skills, and the delivery of HIV education (Nakimuli-Mpungu E et al, *Lancet HIV* 2015;2(5):e190–e199). A form of cognitive behavioral therapy—CBT for adherence and depression (CBT-AD)—also improves depressive symptoms while enhancing adherence with HAART treatment (Safren SA et al, *Health Psychol* 2009;28(1):1–10).

HIV and the brain

In case you've wondered about the acronym "HAND," it stands for HIV-associated neurocognitive disorder and encompasses a spectrum of cognitive and functional impairments:

- Asymptomatic neurocognitive impairment (ANI): mild cognitive impairment but no functional impairment
- Mild neurocognitive disorder (MND): mild to moderate cognitive impairment with some functional impairment
- HIV-associated dementia (HAD): severe cognitive impairment with substantial functional disruption

When working with patients with HIV, you will likely encounter some degree of cognitive impairment. The availability of HAART has decreased the incidence of HIV-associated dementia to about 5%, but the prevalence of MND is largely unchanged, affecting about 45% of infected patients (Bhatia NS and Chow FC, *Curr Neurol Neurosci Rep* 2016;16(7):62). This may be due to patients' longer life spans and continued viral replication in the central nervous system even when serum levels show undetectable viral loads.

Assessment

In cases of mild or moderate neurocognitive impairment, cognitive screening scales may not be sensitive enough to detect deficits. If I suspect mild or moderate cognitive impairment, I usually obtain formal neuropsychological testing to identify specific areas of dysfunction.

HAD, on the other hand, produces prominent symptoms, including decreased psychomotor speed, poor attention, poor concentration, and impaired memory, learning, and executive function (see "Affective, Behavioral, and Cognitive Features of HIV-Associated Dementia" table on page 10). For screening, I recommend the Trail-Making Test as a sensitive and easy-to-use screening tool (www.tinyurl.com/5fx3nw6h). Another instrument, the International HIV Dementia Scale, takes longer to administer but provides a more comprehensive assessment of memory and psychomotor function (www.tinyurl.com/4rmdbbz6).

HAD is a diagnosis of exclusion and thus requires a full workup for other potential causes of the psychomotor slowing (eg, Parkinson's disease). What typical findings might we encounter in our workup? Neuroimaging often shows cerebral atrophy, enlarged ventricles, and T2-hyperintensities in white matter tracts, and an EEG is likely to show mild background slowing—although I don't normally obtain an EEG unless I suspect seizures. A cerebrospinal fluid (CSF) analysis will only show nonspecific findings. There's little reason to obtain a CSF

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Q&A With the Expert

Psychiatric Issues in Organ Transplantation

Paula C. Zimbrean, MD, FAPA, FACLP

Associate professor of psychiatry and surgery (transplant), Yale University School of Medicine; Chair, Transplant Psychiatry Special Interest Group, Academy of Consultation Psychiatry. New Haven, CT.

Dr. Zimbrean has consulted for Ultragenyx and Vivet Therapeutics, and has consulted and advised for Alexion. Relevant financial relationships listed for the author have been mitigated.

CHPR: Please briefly describe the field of transplant psychiatry and what it encompasses.

Dr. Zimbrean: Transplant psychiatrists provide specialized psychiatric evaluations and care for transplant candidates, transplant recipients, and living organ donors. The need for organs in the US far exceeds the availability, so transplant psychiatrists help select the transplant candidates who are most likely to benefit from these scarce resources. Transplant psychiatrists also evaluate living donors to identify psychopathology that can impact the decision to donate or can be worsened by donation. We also educate patients and families about the mental health challenges that come up during the transplantation process. We mostly focus on organ transplantation and vascularized composite allographs (VCAs), such as faces and arms, and not as much on bone marrow transplantation, as those patients are typically followed by psycho-oncology services.

CHPR: Why is it important for hospital and outpatient psychiatrists to know about transplant psychiatry?

Dr. Zimbrean: The number of transplantations grows every year, and transplant recipients increasingly follow up in community mental health practices. Also, transplant candidates and recipients often have significant psychiatric or addictive disorders that led to the indication for transplantation (eg, alcohol-related liver disease or lithium-induced kidney disease).

CHPR: How many transplants are performed in the US?

Dr. Zimbrean: Last year there were over 40,000 organ transplants performed in the US, and for the last decade the numbers have increased every year. Even with the COVID-19 pandemic, which markedly reduced living donations in 2020 (as they were considered elective procedures), the rate of organ transplants continues to grow. Sadly, the availability of organs falls far short of the demand, and thousands of patients die every year waiting for an organ.

"When prescribing for transplant recipients, try to avoid medications with risks of organ toxicity whenever possible and be mindful of drug interactions with immunosuppressant medications."

Paula C. Zimbrean, MD, FAPA, FACLP

CHPR: How long are the waitlists?

Dr. Zimbrean: There are significant geographical disparities in access to transplantation. In general, waitlists are shorter in the South and Midwest and longer on the coasts and in the North. The United Network for Organ Sharing (UNOS)—the organization that oversees organ allocations—is working to reduce these disparities. Waitlists also vary by organ. In Connecticut, the wait for a kidney can be as long as six or seven years. For a liver transplant, the wait time depends in part on the severity of the liver disease. For a heart, on the other hand, at times there are enough organs available to ensure rapid transplantation. In these cases, the challenge for us transplant psychiatrists is that we don't have time to evaluate or prepare the patient. We've had patients who walked into the emergency room with chest pain and over the next two to three weeks underwent heart transplantation and then were discharged home with their lives completely changed, asking "What just happened?!" In these cases, transplant psychiatrists mostly focus on helping patients adapt to their loss of health and function and to their need for lifelong medical care.

CHPR: What are the success rates of different organ transplants?

Dr. Zimbrean: The medical outcomes of transplantation, which include graft survival and patient survival, continue to improve. A summary of rate of transplantation and posttransplant survival can be found on the Health Resources and Services Administration website (https://srtr.transplant.hrsa.gov/annual_reports/Default.aspx). Programs report one-year and five-year survival rates, and in general, one-year survival rates are close to 90% for liver, heart, and organs. For kidneys, they are even higher, around 95%. Survival rates start decreasing five years posttransplantation, especially for lung and heart recipients.

CHPR: Can you describe a recent case in which you were asked to consult on a transplant patient, so we have a clear sense of some of the typical psychiatric issues?

Dr. Zimbrean: I recently consulted on a woman in her late 30s with a history of major depressive disorder and alcohol use disorder (AUD). She had alcohol-related liver cirrhosis that had progressed to the point of requiring a liver transplantation. She suffered from lower-extremity edema and ascites and was undergoing paracentesis (the removal of fluid from the abdomen) every other week. AUDs are the main indication for liver transplants in the US. This patient struggled to maintain sobriety and had lost confidence that she could stay abstinent and that her health would ever improve.

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I met with her several times to identify interventions that would help her achieve abstinence and become a transplant candidate. I started her on acamprosate and connected her to an intensive outpatient dual diagnosis program. She has been abstinent now for about three months and hopefully will continue in her recovery so that she can move forward with the transplant and return to a life without physical illness.

CHPR: How long do patients need to maintain sobriety before they can be candidates for liver transplants?

Dr. Zimbrean: Alcohol relapse after transplantation is linked with higher rates of mortality and graft loss, so for many years, a six-month abstinence from alcohol and other illicit substances was a requirement before receiving a transplant (Kodali S et al, *Alcohol Alcohol* 2018;53(2):166–172). The field is now moving toward considering people who have a shorter abstinence, like three or four months, but who are engaged in counseling and show significant motivation to stay abstinent. Another major change is that patients with acute alcoholic hepatitis—who are typically using alcohol until the day that they are hospitalized with liver failure—can receive a liver transplantation if certain conditions are met, such as committing to lifelong abstinence, having good social support, and agreeing to engage in addiction treatment after the surgery (Jesudian AB et al, *Curr Opin Organ Transplant* 2016;21(2):107–110).

CHPR: Besides a patient's length of sobriety, what other factors do you take into consideration when selecting candidates for liver transplants?

Dr. Zimbrean: First, the patient must have no medical contraindications. In general, patients should have a 50% survival expectation at five years. For instance, someone with active malignancies is not a candidate because their malignancies would be accelerated with the immunosuppression needed after the transplant. We also look at psychiatric comorbidities that could impair a patient's ability to adhere to the complex posttransplant medical care or could be made worse after transplantation by medications, like steroids, or by the life changes that result from the transplantation. As transplant psychiatrists, we help select candidates who are most likely to benefit from the procedure for the longest time.

CHPR: Are there any psychiatric contraindications to being a transplant donor or recipient?

Dr. Zimbrean: There are no formal guidelines about psychiatric contraindications to transplantation. If there is an acute psychiatric illness that interferes with the patient's ability to provide informed consent, and if the transplant is not for a life-threatening condition, then we have time to address the psychiatric condition and discuss the transplant decision later. But if the psychiatric disorder interferes with the patient's ability to participate in the treatment plan, or can be worsened by the transplant, then those patients might not be good candidates. For instance, there are patients with severe bipolar disorder (BPD) who fear a steroid-induced manic episode. Steroids are almost always needed after transplantation, and some patients are so worried about exacerbating their BPD that they decide against kidney transplantation and prefer to continue hemodialysis.

CHPR: What do you do for patients with acute psychiatric illnesses who require a transplant immediately, meaning there's no time to address the psychiatric condition?

Dr. Zimbrean: In these cases, we collaborate with the transplant team and treat the psychiatric condition postoperatively while patients are recovering after transplantation. There are very rare situations when the psychiatric condition is treatment refractory and interferes with a patient's safety or ability to participate in care; in these cases, the transplant team may decide not to proceed with transplantation.

CHPR: How about a history of suicidal ideation or suicide attempts—is that a contraindication?

Dr. Zimbrean: It's an excellent question. If a patient has made multiple suicide attempts despite receiving mental health treatment, and if we feel all interventions have been exhausted and believe the patient is still at high risk for suicide after being discharged from the hospital, then a history of suicidal ideation may be a contraindication. But most commonly we see a different scenario: patients with a remote history of a suicide attempt during a depressive episode who received psychiatric treatment and did well. In these cases, a history of suicide attempt is not a contraindication.

CHPR: What do you look for in evaluations of potential donors?

Dr. Zimbrean: The most common living organ donors are for kidneys, followed by livers. When meeting with the donor candidates, we evaluate for existing psychiatric illnesses that might interfere with the donor's functioning or with their decision to donate. It is also important to ensure the donor can provide informed consent and has realistic expectations about the donation. Another important point is the donor's relationship with the recipient. Prior to the transplantation surgery, some donors have a relationship with the recipient, whereas some don't (so-called "altruistic," "unrelated," or "unaffiliated" donors) and might not desire one. And in some cases we might find out that, consciously or unconsciously, the donor's desire to establish a close relationship is their main motivating drive for offering to donate. In these cases, we help them reach a different resolution for their wishes.

CHPR: What additional information might be helpful for us to know when we encounter transplant patients?

Dr. Zimbrean: Most of the questions I receive from psychiatrists in the community are about what medications are safe to give to transplant recipients. A helpful concept is that if a transplant is successful, the graft works as well as a healthy organ, so usually dose adjustments are not necessary. In addition, we try to avoid medications with risks of organ toxicity (for instance, risk of liver toxicity associated with divalproex) whenever possible and to

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Psychogenic Nonepileptic Seizures

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Dr. Morris has no financial relationships with companies related to this material.

The nurses ask you to see a patient whom they believe is having a seizure. You rush to the patient's room to find her moaning with her eyes closed. Her entire body is shaking, and her movements include pelvic thrusting and arching of her back. You order a dose of intramuscular lorazepam, and she stops moving briefly while the injection is administered. The movements resume for five more minutes, and then the patient sits up and asks for water. The nurses tell you they don't feel comfortable keeping this patient on the psych unit and want her transferred to the medical floor.

Psychogenic nonepileptic seizures (PNES) are paroxysmal events that look like seizures but are not associated with EEG changes. They are also known as psychogenic seizures, dissociative seizures, functional seizures, and nonepileptic seizures. An older term, "pseudoseizure," is no longer in favor as it implies the seizures are feigned. We now know these seizures are not volitional, and the DSM-5-TR classifies PNES as a functional neurologic disorder (conversion disorder). If you've had patients with PNES on your unit, you know their seizure-like episodes take up considerable amounts of time and effort and can be quite distressing to staff and other patients.

The etiology remains unclear, but psychosocial stressors seem to trigger PNES in certain individuals. Patients often have a history of childhood trauma, PTSD, depression, or personality disorders. Additionally, 30% have a developmental disability (Duncan R and Oto M, *Epilepsy Behavior* 2008;12(1):183). Most patients are female and typically first exhibit symptoms in their 20s. The incidence is unclear, but 20%–40% of patients with refractory seizures are eventually found to have PNES (Huff JS and Murr N. Seizure. In: *StatPearls*. StatPearls Publishing; 2022). Conversely, 5%–22% of people with PNES also have epileptic seizures for which they need treatment (Duncan R and Oto M, *Neurology* 2008;71(13):1000–1005).

Typical features and diagnosis

Most cases of PNES resemble tonic-clonic seizures: Patients shake, roll from side to side, and exhibit pelvic thrusting and arching of their backs. These episodes can be dramatic and alarming. If the patient is on your psychiatric unit, you might think they need to be transferred to the medical floor. However, there are clues that can help you distinguish PNES from epileptic seizures.

Emotional vocalizations, like crying or screaming, are common with PNES (see "Differences Between PNES and Epileptic Seizures" table). Patients typically thrash their head and trunk from side to side and keep their eyes tightly closed, in contrast to patients with epileptic seizures. In fact, eye closure predicts PNES in 95% of cases (Chung SS et al, *Neurology* 2006;66(11):1730–1731). Additional features of PNES include asynchronous movement of limbs and the absence of a postictal period. Epileptic seizures are usually brief (less than two minutes), while PNES can last much longer. "Psychogenic status epilepticus" refers to PNES episodes that last 20 minutes or more and can be mistaken for status epilepticus.

Behaviors like tongue-biting and incontinence do not generally help in making the diagnosis. While they are more commonly observed in epileptic seizures, nearly one-third of PNES episodes will present with these behaviors (Reuber M et al, *Ann Neurol* 2003;53(3):305–311).

A minority of patients with PNES don't demonstrate convulsive features but instead have a "swoon" version of PNES, with minimal movement and nonresponsiveness. This variant is more likely to occur in public places, like a doctor's waiting room (Benbadis SR, *Epilepsy Behav* 2005;6(2):264–265).

Diagnosis

Can you conclusively make the diagnosis of PNES if your patient exhibits all the classic features? No—epileptic seizures can be mistaken for PNES, so patients should undergo a full neurologic workup for epilepsy. The gold standard for diagnosis of PNES is long-term video-EEG monitoring (also known as EEG telemetry).

PNES is a diagnosis of exclusion. Other conditions to keep in your differential diagnosis include absence seizures, partial complex seizures, syncope, movement disorders, and sleep disorders (eg, narcolepsy and restless legs syndrome).

Treatment

Once you have determined that your patient's symptoms represent PNES, what do you do next? First and foremost, inform your patient about the diagnosis in a respectful, nonjudgmental manner, acknowledging the distress they feel from their condition. This simple intervention will often put an end to a patient's PNES episodes! Disclosure of the PNES diagnosis resolves symptoms in 17%–40% of patients (Duncan R et al, *Epilepsy Behav* 2020;102:106667). I reassure

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Differences Between PNES and Epileptic Seizures

Feature	PNES*	Epileptic Seizures
Duration	Several minutes	Less than two minutes
Eyes	Closed	Open
Limbs	Out of phase	In phase
Post-ictal confusion	Absent or very brief	Several minutes to hours
Reaction to loud noise or startle stimulus	Yes	No
Thrashing	Side-to-side movements of head and trunk	Leg movements are most common
Vocalization	More frequent with emotional content (crying, screaming)	Monotonous and without emotional content

**Patients with PNES may display some but not all of these features*

Psychogenic Nonepileptic Seizures

Continued from page 9

patients that their test results are normal and tell them that their symptoms are, indeed, real, but do not represent traditional "seizures." I also explain how our bodies sometimes translate trauma and mental distress into physical symptoms.

Another important step is to treat co-occurring psychiatric diagnoses, like depression, anxiety, and personality disorders. Psychotherapy—in particular, cognitive behavioral therapy (CBT)—can be effective in treating or reducing PNES episodes (Goldstein LH et al, *Lancet Psychiatry* 2020;7(6):491–505).

And lastly, discontinue antiepileptic medications in individuals who do not need them. This step can be tricky, as some people with PNES also have epileptic seizures. But if the workup confirms your patient does not have epileptic seizures, there's no reason to expose them to unnecessary treatment. Failure to correctly identify PNES can lead to large administrations of benzodiazepines, respiratory depression, and even death (Reuber M et al, *Neurology* 2004;62(5):834–835).

What's the prognosis?

Unfortunately, about 60% of individuals with PNES will continue to have seizures despite interventions, although treatment helps reduce the frequency. It's not unusual for these patients to remain on psychiatric units for extended periods as their improvement can be slow. Certain demographic factors, including higher education and younger age of symptom onset, portend a more favorable prognosis (Reuber et al, 2003).

You provide an in-service to educate the psych unit staff about PNES. You educate the patient about her symptoms, treat her underlying depression, and encourage her to join a support group, where she works on overcoming maladaptive communication skills. She tells you that she now realizes that she can stop impending episodes by writing in her journal. She feels ready to return home.

CARLAT VERDICT

To identify PNES, look for clues: emotional vocalizations (eg, crying, screaming), closed eyes, thrashing of the head and trunk, and an absence of post-ictal confusion. The gold standard for diagnosis is video-EEG. PNES episodes will often resolve or lessen when patients learn about their diagnosis. Discontinue unnecessary antiepileptic medications, treat co-occurring psychiatric disorders, and refer patients for therapy, like CBT, to help reduce the frequency of events. Remember that some patients with PNES also have epilepsy.

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Management of Depression and Neurocognitive Impairment in Patients With HIV

Continued from page 6

Affective, Behavioral, and Cognitive Features of HIV-Associated Dementia

Affective features	• Apathy • Dysphoria • Psychosis in severe cases
Behavioral manifestations	• Agitation • Insomnia • Lethargy • Social withdrawal
Cognitive features	• Concentration difficulties • Inability to complete multistep activities • Poor attention span • Short-term memory impairment • Visuo-spatial impairment • Word-finding difficulties
Neurological findings	• Disturbances in smooth-pursuit eye movements • Frontal-release signs (primitive reflexes, such as palmar grasp, that are seen in disorders affecting the frontal lobes) • Hyperreflexia • Incoordination • Weakness (worse in the lower limbs)

analysis in most cases, but if a patient's symptoms have progressed rapidly or their CD4 count drops below 100, CSF analysis can help rule out other HIV-related diseases, such as cryptococcal meningitis and toxoplasmosis.

Treatment

The optimal treatment for HAD and HIV-associated neurocognitive disorder is to control viral replication with HAART, as good management of the HIV infection correlates with improved cognitive function (Joska JA et al, *J Neurovirol* 2010;16(2):101–114). No medications are approved for the treatment of HAD/HAND, but medications for comorbid psychiatric symptoms (eg, agitation) can be helpful.

Potential adverse neuropsychiatric sequelae of HAART

If a patient with HIV demonstrates new-onset cognitive changes or psychiatric symptoms, I look for recent changes to their treatment regimen. Several medications for HIV produce neuropsychiatric disturbances, so I encourage my infectious disease colleagues to take these side effects into account when choosing HAART medications (see "Neuropsychiatric Side Effects Associated With Medications Used in HIV/AIDS" table on page 5). This is especially important for patients with a history of preexisting psychiatric disorders or with active, poorly controlled psychiatric symptoms. Raltegravir appears to produce a lower risk of neuropsychiatric side effects compared to other options (Kim MJ et al, *Infect Chemother* 2015;47(4):231–238).

CARLAT VERDICT

Patients with HIV/AIDS are at high risk of depression and suicide, especially in the days following the HIV diagnosis. Many patients with HIV also struggle with cognitive impairment from HAND, and about 5% develop HAD. Psychotherapy and antidepressants help treat patients' moods, and HAART diminishes the risk of cognitive impairment. Watch for drug interactions and neuropsychiatric side effects from antiretroviral medications.

CME Post-Test

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This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Learning Objectives (LO) are listed on page 1.

1. Which medication has been shown to stimulate appetite without producing anticholinergic side effects when treating depression in patients with HIV (LO #1)?
   [ ] a. Mirtazapine
   [ ] b. Bupropion
   [ ] c. Modafinil
   [ ] d. Dextroamphetamine

2. Which of the following would prevent a patient from receiving gender-affirming surgery (LO #2)?
   [ ] a. Symptoms of depression related to the patient's gender dysphoria
   [ ] b. Symptoms of an endogenous major depressive episode
   [ ] c. Neither an endogenous major depressive episode nor depression related to gender dysphoria can prevent a patient from receiving gender-affirming surgery
   [ ] d. A history of depression, now in remission

3. What percentage of patients with psychogenic nonepileptic seizures (PNES) have a developmental disability (LO #4)?
   [ ] a. 10%
   [ ] b. 30%
   [ ] c. 45%
   [ ] d. 65%

4. Which of the following would indicate that a patient is a poor candidate for an organ transplant (LO #3)?
   [ ] a. A 50% survival expectation at five years post-transplant
   [ ] b. A patient's relationship with the organ donor
   [ ] c. Active malignancies
   [ ] d. A psychiatric disorder that is in remission

5. Which rating scale is most reliable in its ability to screen for depression and anxiety in patients with HIV (LO #1)?
   [ ] a. Beck Depression Inventory (BDI)
   [ ] b. Hospital Anxiety and Depression Scale (HADS)
   [ ] c. Columbia-Suicide Severity Rating Scale (C-SSRS)
   [ ] d. Formal neuropsychological testing

6. How do mental health outcomes compare between individuals who receive hormone replacement therapy (HRT) versus surgical procedures (LO #2)?
   [ ] a. HRT leads to improved mental health outcomes compared to surgery
   [ ] b. Surgery leads to improved mental health outcomes compared to HRT
   [ ] c. Neither HRT nor surgery leads to improved mental health outcomes
   [ ] d. Both HRT and surgery lead to comparable mental health outcomes

7. Which of the following is a difference between PNES and epileptic seizures (LO #4)?
   [ ] a. PNES last less than two minutes while epileptic seizures last several minutes
   [ ] b. Patients with PNES typically keep their eyes closed while patients with epileptic seizures keep their eyes open
   [ ] c. Patients with PNES do not react to loud noise, while patients with epileptic seizures do
   [ ] d. Patients with PNES experience synchronous movement of limbs, while patients with epileptic seizures experience asynchronous movement of limbs

8. To be approved for a liver transplant, how long must patients remain sober (LO #3)?
   [ ] a. Two months
   [ ] b. Six months
   [ ] c. Eight months
   [ ] d. One year

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Expert Interview – Psychiatric Issues in Organ Transplantation
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be mindful of drug interactions with immunosuppressant medications.

CHPR: Finally, can you say something about the new types of transplants you mentioned earlier—VCAs?

Dr. Zimbrean: These transplants improve quality of life, but they are not lifesaving, so the decision process is different. In many cases the need for the transplant is due to a traumatic injury, for example from a gunshot to the head in a suicide attempt. Patients require many procedures before the transplant procedure and almost invariably become dependent on opioids iatrogenically because they need them for pain control. In addition, the typical doses of immunosuppressant medications for VCAs are higher than for organ transplants, so they risk more side effects. Rejection is also different: While organ recipients with rejection become ill and are hospitalized, the rejection of a VCA is more localized, and patients may see their body part literally decaying. Seeing one's own face going through rejection—changing color, necrotizing—that is another trauma. On the other hand, quality of life can improve so much afterward that I think these types of transplants will become more widespread.

CHPR: Thank you for your time, Dr. Zimbrean.

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