

Case Report

Gender Dysphoria Versus Acute Psychosis: Can One Properly Diagnose Gender Dysphoria Solely During Acute Psychosis?

Kristy A. Fisher, MD, MS, MBA¹; Samantha Scemla, BA²;
Clara L. Alvarez Villalba, MD¹; Jessica Kroin, MD, MS¹

Abstract

Description

Gender dysphoria occurs when a discrepancy between one's sex assigned at birth and one's gender identity causes distress or impairment in function, which can lead ultimately to seeking treatment in the forms of psychotherapy, hormonal therapy, and/or gender-affirming surgery. Clinical care guidelines also recommend pharmacological treatment of psychiatric comorbidities if indicated. A review of the current literature demonstrates comorbidity between gender dysphoria and psychosis, including cases of gender dysphoria with schizophrenia and the occurrence of gender dysphoria symptoms during manic or psychotic episodes. The existing literature has yet to specifically examine gender dysphoria amongst individuals with schizoaffective disorder. The authors present the first documented case of a clear pattern of gender identity variations coinciding solely with psychotic episodes during schizoaffective disorder, bipolar type. The authors postulate that gender dysphoria can co-occur with other psychiatric disorders or may correspond only during acute psychosis. The distinction is critical to make to ensure accurate diagnoses regarding whether gender dysphoria is a symptom only during an acute psychotic illness, or if there is a longer-standing concern as to the patient's gender identity and assignment. This distinction then also informs how to make the most appropriate treatment recommendations. The authors address the significance of understanding each patient's individual circumstances and deem this paramount to advancing transgender and gender non-binary health equity at every level of medical attention, focusing specifically on proper physician training and direct patient care.

Keywords

gender dysphoria; gender identity disorder; transgender; schizophrenia; psychological sexual dysfunctions; sexual behavior; psychiatric symptoms; psychotic disorders; transgender persons/psychology; transsexualism; health services for transgender persons

Introduction

Gender dysphoria is the distress or discomfort that occurs when there is a discrepancy between one's sex assigned at birth and one's gender identity. This discomfort can ultimately lead to seeking treatment in the forms of psychotherapy, hormonal therapy, and/or gender-affirming surgery, as well as pharmacological management of psychiatric comorbidities as appropriate.^{1,2} A review of the current literature reports patient cases of gender dysphoria comorbid with schizophrenia, as well as gender dysphoric presentation during manic or psy-

chotic episodes.^{3,4} Studies demonstrate up to 25% of patients with schizophrenia experience signs of gender dysphoria throughout their lives, including beliefs regarding belonging to another gender.² Gender dysphoria occurring solely during psychotic breaks exclusively with schizoaffective disorder, and a progressively intensifying identification with a different gender associated with acute schizoaffective illness has not been documented in the literature. However, overlapping polygenetic and environmental contributions to schizophrenia and bipolar disorders is possible.

Author affiliations are listed at the end of this article.

Correspondence to:
Kristy A. Fisher, MD, MS
MBA
HCA Florida Aventura
Hospital
20900 Biscayne Blvd
Aventura, FL 33180
(Kristy.Fisher2@hcahealthcare.com)

Most presentations of gender dysphoria are not difficult to diagnose.⁵ However, for unique presentations of gender dysphoria—particularly those with co-existent psychiatric conditions—challenges in diagnosis can occur. Per the World Professional Association for Transgender Health (WPATH) Guidelines for treatment, to obtain hormone replacement therapy (HRT), patients must demonstrate a capacity to make well-informed decisions, exemplify persistent and well-documented gender dysphoria, and all additional medical, physical, and mental health concerns should be considered medically stable.^{6,7} Additionally, if a patient seeks surgical treatment in the form of chest reconstruction or other non-genital procedures, the patient additionally requires 1 letter from a mental healthcare provider. If the patient desires genital reconstructive surgery, 1 full year of continuous hormone therapy, along with 2 letters from two separate healthcare providers, is required.⁶⁻⁸

There is a paramount need for expansion of awareness, knowledge, and experience with gender dysphoria, for both general practitioners and general psychiatrists, to ensure a proper diagnosis and equitable and appropriate treatment. Health equity is the principle underlying a commitment to minimize, and ultimately eliminate, disparities in health and its social determinants.⁸ Striving for health equity requires striving for the highest possible standard of health for all and providing special consciousness to the needs of those at the greatest risk of poor health as a result of social, economic, and environmental conditions. In making health equity a shared vision and value, it is possible to foster equal opportunity for health, the foundation for a vigorous and healthy community.⁹ Understanding each patient's individual circumstances is crucial to advancing health equity at every level of medicine. Given the growing body of evidence of extreme health inequity among patients who are gender diverse, it is essential to explore case presentations of those who present with both typical and unique presentations of gender dysphoria.^{4,10}

Case Description

In this case report, the patient will be referred to without using pronouns given fluctuations

in pronouns over time. A 35-year-old Hispanic person, assigned male at birth, identified as female upon admission. The patient denied any significant or contributing past medical history. The patient had a past psychiatric history of schizoaffective disorder, bipolar type, and presented involuntarily to the psychiatric inpatient unit for bizarre behavior and auditory hallucinations for the past three months. Per the patient's mother's report, the patient had been refusing to eat, was easily agitated, and was exhibiting signs of mania, including decreased sleep, and increased sexual behavior. The patient reported medication nonadherence for an unknown amount of time. The patient denied the previous existence of a female identity. Upon admission, the patient presented in masculine clothing and identified as a female, requesting that staff use she/her/hers pronouns.

Social Context: The patient was an only child and lived with the patient's mother in a single-family home. The patient was unemployed at the time of admission. The patient's highest level of education was a high school diploma. The patient refused to discuss sexual orientation but did disclose having sexual relations with men and women. The patient denied a history of trauma or experiences of discrimination. The patient also denied a family history of psychiatric illness or gender dysphoria.

Collateral (reported by patient's mother):

The treating physician perceived the patient's mother's perspective of fluctuations in gender identity to be neutral. In other words, the patient's mother did not express any explicitly anti-transgender attitudes. The patient's mother reported that with all psychotic breaks since the age of 21 (age of first psychotic break), the patient identified as a female, with an immediate reversal to male identification upon stabilization of the acute psychosis. Prior to this age, no gender nonconformity was revealed to the mother by the patient nor did the patient's mother ever discuss or address gender nonconformity with the patient. The patient's mother reported that during a previous psychotic break, the patient identified as female. The patient survived a serious opioid overdose that had resulted in a coma of 13-days duration. Upon awakening and with medical stabilization, the patient immediately transitioned to a male

Table 1. DSM-5 Diagnostic Criteria for Gender Dysphoria in Children and Adults¹¹

Gender Dysphoria DSM V Diagnostic Criteria	
Children (6/8 required for at least 6 months)	Adults (2/6 required for at least 6 months)
<ul style="list-style-type: none"> • Desire to be or insistence that one is another gender (required for diagnosis) • Wearing opposite gender clothes • Preferring opposite gender roles at play-time • Preferring toys/games/activities of opposite gender • Preferring playmates of opposite gender • Rejection of toys/games/activities typical of native gender • Strong dislike of sexual anatomy • Desire for primary and/or secondary sexual characteristics of experienced gender 	<ul style="list-style-type: none"> • Incongruence between primary/secondary sexual characteristics of one's natal gender and that of experienced gender • Desire to avoid or be free of the sexual characteristics of natal gender • Longing for sexual characteristics of another gender • Longing to be treated as another gender • Believing that their feelings and/or reactions are of another gender

identity. Upon returning home from the hospital, the patient got a crew cut and threw out all feminine products and décor. The patient's mother expressed that the patient was very troubled by the changes throughout each psychotic break. Upon recognizing a clear pattern, the patient's mother began saving and storing all female clothing, accessories, and décor in the attic for future use. With each successive break, the patient's presentation exhibited a progressive nature, commencing with laser body hair removal, then feminizing hormone therapy, then obtaining one of two required letters for gender-affirming genital surgery. Each successive break did show a lengthening in time and an increase in severity. There were a total of 5 psychotic breaks.

Physical Examination

General Assessment: Upon initial assessment, the patient appeared thin and frail, and exhibited extreme emotional lability.

Vital Signs: Heart Rate: 97 beats per minute, Respiratory Rate: 18 breaths per minute, Blood Pressure: 110/71mmHg, O2 Saturation: 98%
BMI: 20

Examination: Unremarkable

Labs: WNL

Urine Drug Screen: Negative

Blood Alcohol Level: WNL

Std Panel: Negative

HIV: Negative

Treatment

Risperidone 0.5 mg twice daily and valproic acid 500 mg twice daily were initiated. Risperdal was titrated up to 1.0 mg twice daily over

the course of the hospitalization. Group and individual therapy were provided, and a family session was held to ensure a safe discharge home. The patient's condition stabilized over the course of the hospitalization, the patient no longer identified as a female and requested that the mother bring male clothing. All psychotic symptoms including hallucinations resolved completely. The patient was discharged after 8 days of hospitalization, with follow-up recommended. To this date, the patient has not presented back to this hospital.

Discussion

This case presentation extends a sparse literature concerning progressive episodes of gender dysphoria coinciding solely with psychotic breaks of schizoaffective disorder, bipolar type. No studies have yet examined gender dysphoria symptoms occurring in the context of psychosis among individuals with schizoaffective disorder, as it tends to not be seen or correctly identified routinely in clinical practice. This case presentation suggests that gender dysphoria can have a complex interrelationship with comorbid disorders, such as schizoaffective disorder. Additionally, this report demonstrates the patient's continuity of transgender identity across psychotic episodes. The authors review neurobiological research as well as identify challenges in diagnosing gender dysphoria (Table 1) and ensuring appropriate treatment (Table 2), provide suggestions on addressing these challenges, and discuss the significance of a thorough history evaluation and collection of collateral information.

Table 2. Criteria for Initiation of Hormonal and Surgical Treatment with Gender Dysphoria¹²

Treatment	Criteria for initiation
Hormonal therapy	<ul style="list-style-type: none"> • Persistent and well-documented gender dysphoria • Capacity to make well-informed decisions • Other medical and mental health issues are well controlled
Surgical treatment	<ul style="list-style-type: none"> • Same as above, plus: • 1 year of continuous hormone therapy and 1 year living as desired gender (unless not medically indicated) <p>*Not required for chest reconstruction or non-genital surgeries</p> <ul style="list-style-type: none"> • Chest Surgery: 1 letter from mental healthcare provider • Genital Surgery: 2 letters from separate mental healthcare providers

The literature indicates a significant comorbidity between schizophrenia and gender dysphoria. Much of the literature suggests that a diathesis-stress model accounting for minority stress experienced by gender minorities may explain this comorbidity.^{4,13} Some neurobiological research also suggests neurobiological underpinnings for both mental health concerns. Altered cerebral sexual dimorphism, or gender-atypical brain development (differing from normal gender-specific brain development) may be caused by differences in prenatal hormones and changes in cerebral lateralization.^{14,15} In individuals with gender dysphoria, brain imaging studies demonstrate dimorphic brain regions that reflect gender identity, rather than anatomical sex (conventionally, larger volumes of gray matter are seen within the left hemisphere in a male brain, while larger volumes of gray matter are seen in the right hemisphere of a female brain).^{14,16} Some brain structures of individuals with schizophrenia demonstrate a similar variation, where brains of cisgender women with schizophrenia follow patterns that are typical for cisgender men and brains of cisgender men with schizophrenia follow patterns that are typical for cisgender women.¹⁴⁻¹⁶ Thus, it is possible that fetal processes of neurodiverse brain development—influenced by prenatal hormones—affect the later expression of schizophrenia and gender dysphoria (as well as a host of other developmental and mental health concerns, such as autism spectrum disorder).²

Additionally, several findings suggest a non-normative pattern of cerebral lateralization and handedness in individuals with schizophrenia as well as those with gender dysphoria.¹⁷ A recent meta-analysis found that individuals with schizophrenia had a higher

incidence of left-handedness.¹⁷ Correspondingly, a recent study found that AMAB (assigned male at birth) individuals with gender dysphoria demonstrated a significantly higher rate of left-handedness.¹⁸ This common finding could suggest a similar non-normative pattern of lateralization in both schizophrenia and gender dysphoria.

Neurobiological research also indicates common comorbid diagnoses between both schizophrenia and gender dysphoria, including *Toxoplasma gondii* infection/inflammation, autism spectrum disorders (ASD), and reduced serum brain-derived neurotrophic factor (BDNF).^{15,19} Although they are distinct mental health concerns, ASD and schizophrenia substantially overlap on anatomical and neurocognitive aspects of the brain.¹⁵ Similar to schizophrenia, ASD is linked to differences in prenatal testosterone exposure, which is relevant to the nature of gender dysphoria.¹⁵ Additionally, a family history of schizophrenia is a known predisposing factor for ASD, implicating a genetic link between the two.^{19,20} Decreased levels of BDNF were found in a recent controlled study of 45 male-to-female patients above the age of 18 with gender dysphoria compared with 66 healthy male controls,²¹ hypothesized as consistent with psychological abuse, as exclusion criteria included the presence of a comorbid psychiatric disorder.²¹ Such findings suggest an overlap in common biochemical pathways of neuroplasticity, as well as both inherited and acquired differences in brain development.

Unfortunately, it holds true that individuals who fall outside of conceptions of “normality” are deemed internally pathological, leading to stigmatization, with resultant tribulation.²² To best support affected individuals, a more

thoughtful approach would be to replace the “disability” or “illness” paradigm with a “diversity” perspective, which in turn would consider strengths, weaknesses, and the idea that variation can be positive in and of itself.²² Additionally, the language used to discuss this neurodiversity must be supportive of those living with schizophrenia, schizoaffective disorder, and gender dysphoria, rather than stigmatizing language. Lastly, it is crucial to stray away from the usage of the term “normal” when referring to the brain and mind.²³

The co-occurring nature versus the consequential nature of gender dysphoria with psychotic and/or mood disorders poses challenges in proper diagnosis and appropriate treatment choices. A review of the current literature reports cases of both schizophrenia along with gender dysphoria, as well as gender dysphoria during mania, with up to 25% of patients living with schizophrenia experiencing positive signs of gender dysphoria throughout their lives.^{2,4} Distinguishing between both possibilities is a diagnostic challenge, yet a fundamental process affecting therapeutic decision-making. Before designating treatment options, a thorough diagnostic evaluation should occur, with the patient’s decision-making capacity being well-established. Moreover, the unique physical, mental, and social needs of this particular patient population must be taken into consideration, especially to avoid any medical barriers. Therefore, there is a considerable need to expand the awareness and knowledge of and experience with gender dysphoria patients, for both general practitioners, as well as general psychiatrists. Distinguishing between accurate diagnoses of gender dysphoria is vital to ensure that individuals receive proper care and management in each unique case, incorporating all treatment leading up to and including gender reassignment surgery. Thorough diagnostic evaluations, physical exams, and the collection of collateral information are all crucial factors in diagnostic work-up and treatment planning. Additionally, as per WPATH, the patient’s capacity to make decisions should be well-established before proceeding with all plans for treatment.

This case demonstrated consistent female identity with continuity across manic episodes, from seeking laser body hair removal early on,

to hormonal replacement therapy with later episodes, and finally to obtaining 1 of 2 required letters for sexual reassignment surgery. To the authors’ knowledge, this case depicts the first documentation of such a presentation. The authors postulate long-term antipsychotic use as a major contributing factor, due to the up-regulation of D2 receptors and subsequent dopamine receptor supersensitivity, leading to compensatory dopamine overactivity when off D2-blocking medication, with resultant worsening of positive symptoms of psychosis.²⁴

Conclusion

This case presentation depicts a clear pattern of gender identity change from male to female coinciding solely with psychotic breaks of schizoaffective disorder, bipolar type. The authors postulate that gender dysphoria can co-occur with other psychiatric disorders or as a direct result of acute psychosis. It is important to note the distinction between “gender dysphoria” and “transgender/gender non-binary identity”. As stated above, gender dysphoria occurs when a discrepancy between one’s sex assigned at birth and one’s gender identity causes distress or impairment in function while transgender/gender non-binary identity is an umbrella term for people whose gender identity is different from the sex assigned to them at birth. It is important to note that one can occur without the other and not everyone with gender dysphoria symptoms would benefit from HRT, surgery, or other gender-affirming interventions. On the other hand, many transgender individuals and gender non-binary individuals who do not meet the criteria for gender dysphoria may benefit considerably from gender-affirming treatments. Additionally, the authors consider that it would be noteworthy to study gender variance during the various stages of schizoaffective disorder to better understand if gender dysphoria tends to occur more during periods of psychotic episodes versus mood episodes.

The authors emphasize the critical importance of distinguishing between the two presentations of gender dysphoria (co-occurring with psychiatric disorders or as a direct result of acute psychosis) to ensure an accurate diagnosis before proceeding with treatment for gender concerns. A thorough diagnostic evalu-

ation, physical examination, and the collection of collateral information are all necessary steps in the proper diagnosis and the allocation of treatment planning. Additionally, the patient's capacity to make decisions should be well-established before proceeding with any plans for treatment. Furthermore, emphasis should be placed on the consideration of each case on an individual basis with unique needs as the field of medicine moves briskly towards recognizing health equity at every level of medical attention.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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Author Affiliations

1. HCA Florida Aventura Hospital, Aventura, FL
2. Syracuse University, Syracuse, NY

References

1. Atkinson SR, Russell D. Gender dysphoria. *Aust Fam Physician*. 2015;44(11):792-796.
2. Stusiński J, Lew-Starowicz M. Gender dysphoria symptoms in schizophrenia. Objawy dysforii płci w schizofrenii. *Psychiatr Pol*. 2018;52(6):1053-1062. doi:10.12740/PP/80013
3. Heare MR, Barsky M, Faziola LR. A case of mania presenting with hypersexual behavior and gender dysphoria that resolved with valproic acid. *Ment Illn*. 2016;8(2):6546. doi:10.4081/mi.2016.6546
4. Meijer JH, Eeckhout GM, van Vlerken RH, de Vries AL. Gender dysphoria and co-existing psychosis: review and four case examples of successful gender affirmative treatment. *LGBT Health*. 2017;4(2):106-114. doi:10.1089/lgbt.2016.0133
5. Byne W, Karasic DH, Coleman E, et al. Gender dysphoria in adults: an overview and primer for psychiatrists. *Transgend Health*. 2018;3(1):57-70. doi:10.1089/trgh.2017.0053
6. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2017;102(11):3869-3903. doi:10.1210/jc.2017-01658
7. Ristori J, Steensma TD. Gender dysphoria in childhood. *Int Rev Psychiatry*. 2016;28(1):13-20. doi:10.3109/09540261.2015.1115754
8. Braveman P. What are health disparities and health equity? We need to be clear. *Public Health Rep*. 2014;129 Suppl 2(Suppl 2):5-8. doi:10.1177/003335491412915203
9. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Baciu A, Negussie Y, Geller A, et al., eds. *Communities in Action: Pathways to Health Equity*. Washington (DC): National Academies Press; January 11, 2017.
10. Su D, Irwin JA, Fisher C, et al. Mental health disparities within the LGBT population: a comparison between transgender and non-transgender individuals. *Transgend Health*. 2016;1(1):12-20. doi:10.1089/trgh.2015.0001
11. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. American Psychiatric Association Publishing; 2013. doi:10.1176/appi.books.9780890425596.
12. Tangpricha V, Safer D. Transgender Men: Evaluation and Management. *UptoDate*. Accessed May 27, 2022. <https://www.uptodate.com/contents/transgender-men-evaluation-and-management/>
13. Smith WB, Goldhammer H, Keuroghlian AS. Affirming gender identity of patients with serious mental illness. *Psychiatr Serv*. 2019;70(1):65-67. doi:10.1176/appi.ps.201800232
14. Oertel-Knöchel V, Linden DE. Cerebral asymmetry in schizophrenia. *Neuroscientist*. 2011;17(5):456-467. doi:10.1177/1073858410386493
15. Rajkumar RP. Gender identity disorder and schizophrenia: neurodevelopmental disorders with common causal mechanisms?. *Schizophr Res Treatment*. 2014;2014:463757. doi:10.1155/2014/463757
16. Ristori J, Cocchetti C, Romani A, et al. Brain sex differences related to gender identity development: genes or hormones?. *Int J Mol Sci*. 2020;21(6):2123. doi:10.3390/ijms21062123
17. Brandler WM, Paracchini S. The genetic relationship between handedness and neurodevelopmental disorders. *Trends Mol Med*. 2014;20(2):83-90. doi:10.1016/j.molmed.2013.10.008
18. Zucker KJ, Beaulieu N, Bradley SJ, Grimshaw GM, Wilcox A. Handedness in boys with gender identity disorder. *J Child Psychol Psychiatry*. 2001;42(6):767-776. doi:10.1111/1469-7610.00773

19. Yolken RH, Dickerson FB, Fuller Torrey E. Toxoplasma and schizophrenia. *Parasite Immunol.* 2009;31(11):706-715. doi:10.1111/j.1365-3024.2009.01131.x
20. Sullivan PF, Magnusson C, Reichenberg A, et al. Family history of schizophrenia and bipolar disorder as risk factors for autism. *Arch Gen Psychiatry.* 2012;69(11):1099-1103. doi:10.1001/archgenpsychiatry.2012.730
21. Fontanari AM, Andreazza T, Costa ÂB, et al. Serum concentrations of brain-derived neurotrophic factor in patients with gender identity disorder. *J Psychiatr Res.* 2013;47(10):1546-1548. doi:10.1016/j.jpsychires.2013.04.012
22. Chapman R. Neurodiversity theory and its discontents: autism, schizophrenia, and the social model of disability. In: Bluhm R, ed. *The Bloomsbury Companion to Philosophy of Psychiatry.* Bloomsbury Academic; 2019:371-90. doi:10.5040/9781350024090
23. Armstrong T. The myth of the normal brain: embracing neurodiversity. *AMA J Ethics.* 2015;17(4):348-352. doi:10.1001/journalofethics.2015.17.4.msoc1-1504
24. Chouinard G, Samaha AN, Chouinard VA, et al. Antipsychotic-induced dopamine supersensitivity psychosis: pharmacology, criteria, and therapy. *Psychother Psychosom.* 2017;86(4):189-219. doi:10.1159/000477313