

All Psychosis is Not Schizophrenia, Especially Not in Women

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Abstract

Background: The twelve-month stability of a diagnosis of schizophrenia after a first episode of psychosis is higher in men than in women. **Purpose:** To explore confounding conditions that exist in women. **Method and Results:** Review of recent literature on psychosis associated with starvation, diet aids, immune disorders, steroid use, estrogen withdrawal, thyroid conditions, abuse of domestic solvents, Turner Syndrome, depression, sleep deprivation, and posttraumatic stress. **Conclusion:** Clinicians need to screen for conditions prevalent in women that can induce psychosis and mimic schizophrenia. This will diminish erroneous diagnosis and inappropriate treatment.

Key Words: Schizophrenia, Women, Atypical Psychosis, Anorexia Nervosa, Steroid Psychosis, Autoimmune Disease

Introduction

When women present with a psychotic episode, the precise diagnosis is more difficult to make than in men and, when made wrongly, may lead to inappropriate treatment. Many conditions that masquerade as schizophrenia need to be ruled out when the patient is a woman (1). It is important for clinicians to screen for these conditions when assessing women presenting with psychosis. Antipsychotic medications are not innocuous and are best avoided if not specifically indicated. Moreover, the diagnosis of

schizophrenia carries a stigma with far-reaching repercussions and should not be made hastily. This paper reviews nonschizophrenia diagnostic possibilities to be considered when a woman presents with psychotic symptoms.

Starvation-Induced Psychosis

Starvation can lead to psychotic symptoms (2, 3). An estimated 0.5 percent to 3.7 percent of women in North America, convinced they are too fat, deliberately starve themselves in an attempt to lose weight. Anorexia nervosa is nine times more common in women than in men (4).

Eighty-three percent of American college women diet (5) so that, while not starving, a large number may be missing essential nutrients in their diet. The link between essential nutrients and psychosis is reflected in the high ratio of psychosis in celiac disease (6), in vitamin B3 deficiency (pellagra) (7) and in vitamin B12 deficiency where mental or psychological changes can precede hematological signs by many months (8), making this a difficult diagnosis to make

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without an initially high index of suspicion and careful history taking and examination. (See Table 1.)

More likely to cause psychosis than the deficiencies themselves are the effects of weight loss products used, with ever greater frequency, among young women to maintain a body shape that reflects the current cultural ideal.

Table 1	Work Up for Starvation and Nutrient-Deficiency Psychosis
History	Ask about current weight, highest weight, lowest weight, exercise habits, menstrual cycles, eating habits, presence of self-induced vomiting/binge eating, medications.
Physical	Examine for evidence of emaciation, hypothermia, peripheral edema, hair loss, parotid gland hypertrophy, dental enamel erosion, bradycardia, hypotension, dry skin, lanugo, poor skin tone, neurological signs.
Lab Tests	Check for hypokalemia, hypocalcemia, hyponatremia liver function, complete blood count, chest X-Ray for osteopenia, occult blood in feces, ECG.
Treatment	Electrolyte repletion, feeding and supplementation, nutritional counseling, psychotherapy, education, treatment of accompanying depression, family counseling.

Diet Aid Psychosis

Almost one third of college women in the United States report the use of diet aids (9). In an attempt to facilitate weight loss, over-the-counter (OTC) and prescription diet pills, as well as herbal and thyroid supplements, are being used by dieting women to increase their basal metabolic rate; i.e. use up more calories. Significant central nervous system effects can result, including psychosis. The most likely products to cause psychotic manifestations are those containing ephedrine or phenylpropanolamine (PPA). Clinicians need to inquire about these because teenage girls do not volunteer such information to either family members or physicians, and routine blood screening does not test for OTCs. PPA is an ingredient found in many popular OTC diet aids and in oral nasal decongestants. Ephedrine (Ma huang) has become one of the most widely used constituents of diet drugs. Herbal “fen-phen” products that mimic the action of the now banned phentermine contain ephedrine (10) and can cause psychosis (11, 12).

Young women also take high doses of cough and cold medicines in an effort to lose weight. In addition to traditional cough syrup forms, dextromethorphan is being sold over the Internet in powder, capsule, and pill forms. A single dose of 240 to 1500 mg can cause psychodelic effects that mimic psychosis, especially in the approximately 5% of persons of European ethnicity who lack the ability to metabolize the drug normally. Effects include visual, tactile and auditory hallucinations, impaired judgment and mental performance, euphoria, paranoia, and disorientation (13-16).

Caffeine-Induced Psychosis: Caffeine-containing products are also used to assist with weight loss. Caffeine acts as an appetite suppressant and can increase the metabolic rate. At the same time, it is a diuretic, decreasing water retention and leading to instant (but temporary) weight loss (17). Psychosis can result from large doses (18, 19).

Methylphenidate Psychosis: Methylphenidate used for the treatment of attention-deficit hyperactivity disorder is another stimulant that reduces appetite and is used by teenage girls for purposes of losing weight. Methylphenidate tablets can be taken orally, or they can be crushed and the powder injected or snorted, producing agitation, hallucinations, and other manifestations of psychosis (20, 21).

Anabolic Steroid Psychosis: Though more male athletes than female athletes use anabolic steroids as performance enhancers, young women increasingly are using them to lose body fat (22). The deleterious effects of anabolic steroids, sometimes called “roids rage,” include volatile mood, paranoia, and aggression (23, 24).

Investigation consists of asking about the use of these products in the context of weight control and dietary history. Short-term use of antipsychotic medication may be necessary during the withdrawal period.

Autoimmune Disorders

Quite apart from women’s socially-derived pressure to be slim, there are biologic immune differences between the sexes that make women especially vulnerable to autoimmune disorders (nearly 79% of autoimmune disease patients are women), and these disorders, as well as their treatment, can manifest as psychosis (25, 26). Multiple sclerosis (MS) is an example; it is one of the most prevalent neurological causes of progressive disability in early-to-middle adulthood, affecting approximately 100 to 300 per 100,000 persons in the United States, more common in women than in men, and sometimes accompanied by signs of psychosis. A psychotic episode can be the presenting sign of MS (27, 28) and, for this reason, all first-episode psychosis patients who show neurological signs are well-advised to undergo a magnetic resonance scan to rule it out (29).

The prevalence of any of the thirty-one diseases usually classified as autoimmune is more than 5%, with extensive comorbidity across diseases (30). Psychosis has been reported in polyarteritis nodosa (31), in antiphospholipid syndrome (32), and in Sjögren’s syndrome, an autoimmune disease nine times more common in women than in men (33). Another autoimmune disorder much more commonly found in women than men is systemic lupus erythematosus (SLE). Whereas males with SLE suffer more from seizures, peripheral neuropathy, severe renal disease and cardiorespiratory involvement, women with SLE experience more headaches and psychiatric symptoms (34). In pediatric and adolescent

patients, psychosis is reported in 12% of prospectively ascertained cases (35). A recent epidemiological study from Denmark found a high prevalence of autoimmune disorder, especially thyrotoxicosis, celiac disease, acquired hemolytic anemia, interstitial cystitis, and Sjögren's syndrome, among those with schizophrenia and also among their relatives (36). Because the association was found among relatives, as well as patients, it is not possible to say that the disease, or its treatment, contributed to the diagnosis. This issue remains inconclusive.

Immunomodulators

Treatment of multiple sclerosis by interferon-beta (IFN-beta) can lead to psychosis, as described by Goeb et al. (37). Psychiatric side effects are widely reported with IFN-alpha but have not yet been fully established with INF-beta. Roughly one third of patients treated with INT-alpha develop psychological problems, including psychotic disorders with paranoid delusions that disappear when treatment is discontinued (38).

Corticosteroids

Steroids used to treat immune disorders have a long and well-documented history of triggering psychotic symptoms. The incidence of a severe psychosis while on oral prednisone ranges from 1.6% to 50%, with a weighted average of 5.7%. Patients at greatest risk are those receiving daily doses greater than 40 mg of oral prednisone or its equivalent, especially during the first five days of treatment. The average daily dose of steroids for patients who develop psychosis is 59.5 mg/day. Steroid psychoses are twice as likely to occur in females as in males, but if one corrects for the higher incidence in females of the disorders for which steroids are prescribed, particularly systemic lupus erythematosus and rheumatoid arthritis, then the total incidence of steroid-induced psychosis per person treated shows only a slight female predominance (39). Steroid creams absorbed through skin and inhaled and intranasal corticosteroids in their new and more potent chlorofluorocarbon (CFC)-free formulations can have systemic effects (40). Sensitization to psychosis may appear after repeated use (41).

The use of corticosteroids in all their many forms needs to be inquired about during assessment for psychosis.

Antiinflammatories

The overall (males and females) relative risk of antipsychotic drug use in users of nonsteroidal antiinflammatory drugs (NSAIDs) has been found to be *lower* than in controls but this is true for men only. The risk is raised in women (42). Cyclo-oxygenase-inhibitors (COX-2 inhibitors) such as rofecoxib can induce visual and auditory hallucinations (43). Indomethacin use postpartum has been reported to induce dizziness, anxiety, fear, agitation, affective lability,

depersonalization, paranoia, and hallucinations. It has been proposed that postpartum women are at particular risk for such reactions because of dopamine supersensitivity exacerbated by prostaglandin inhibition (44).

Gonadal Steroids

Women may also be vulnerable to the central nervous system effects of fluctuations in gonadal steroids, both endogenous and exogenous. Psychosis (auditory hallucinations and delusions of reference) can follow upon estrogen withdrawal due to ovariectomy, contraceptive pills or Premarin injections, hormone replacement therapy, menopause, premenstrual, postpartum, or postabortion withdrawal (45, 46). Postpartum psychosis is well known to clinicians and always checked for in a psychiatric assessment, but the other forms of estrogen withdrawal may go unrecognized. Postpartum psychosis occurs in 1 to 2 cases per 1,000 live births, usually within the first four weeks after delivery (47).

Thyroid Conditions and Thyroid Treatment

All thyroid conditions are more common in women than in men and are generally part of the differential during a psychiatric assessment for psychosis. Whether naturally-occurring or iatrogenic, either insufficient thyroid or too much thyroid can lead to psychotic manifestation (48-51). The tests used to screen for thyroid conditions include: TSH, total T4 and T3, free T4 index.

Substances of Abuse

Substance use and abuse is always investigated when an individual presents with psychosis because substances used for recreational purposes are known to lead to psychosis either during intoxication or upon withdrawal (52). The association is more commonly found in men than in women but what is frequently overlooked is the abuse of household substances, solvents and inhalants, where the rate of experimental misuse is at least as common in women as in men.

Survey results consistently show that nearly twenty percent of high school students have experimented with inhaled substances (53, 54). For substances used by adolescent girls that are inhaled and can lead to psychosis, see Table 2.

Depression, Anxiety and their Treatment

Women suffer more often than men from depression and anxiety. This is commonly known and always considered when making an initial diagnosis. Depression with psychotic features is the main condition to be ruled out when assessing for schizophrenia (55). Less appreciated is the fact that treatment for depression and anxiety can lead to psychotic symptoms through individual susceptibility (56-58) or withdrawal effects (59-62). Bupropion in particular is

implicated in antidepressant-induced psychosis, and withdrawal psychoses appear most often upon withdrawal from monoamine oxidase inhibitors and propranolol.

False eyelash and fingernail adhesives	Shoe polish
Fingernail hardener	Wood varnish and remover
Polish and polish remover	Room deodorizers
Hair and deodorant sprays	Disinfectant sprays
Window cleaners	Aerosol cooking sprays
Frying pan coatings	Whipped cream sprays
Aerosol leather coatings	Stain remover
Stain-proof coatings	Felt-tip markers
Copier, printer, and typewriter correction fluid and thinner	

Sleep Deprivation and its Treatment

Women are twice as likely as men to have difficulties with sleep. This is probably due to a combination of stress and changes in hormonal levels. Difficulty falling asleep, nighttime waking, difficulty waking up, and daytime sleepiness all are linked to premenstrual changes. Sleep deprivation can sometimes lead to psychosis (63) and has often been implicated as a contributory cause of postpartum psychosis (64-66). Treatment with nonbenzodiazepine hypnotics has been reported to cause psychotic reactions in individuals with no prior psychiatric history. The reaction stops with discontinuation of the hypnotic agent (67-68).

Genetic Syndromes

Turner Syndrome (TS) is a relatively common genetic syndrome resulting from a 45XO or 45XO/46XX mosaic karyotype. The phenotype includes mild psychosis precipitated by stress, prominent mood features, and some features of organic disease (69). Treatment of psychosis associated with TS requires antipsychotic medication.

Posttraumatic Stress Syndrome Disorder (PTSD)

Psychotic features, including auditory and visual hallucinations and paranoid delusional thinking, are frequent in combat veterans, showing that psychotic symptoms may arise from stress. Such symptoms are best treated without antipsychotic medication together with the psychological interventions effective for PTSD (70). (See Table 3.)

Clinicians need to suspect PTSD whenever the person has been exposed to a traumatic event and continues to re-experience it, while also avoiding all reminders of the trauma

and displaying a general emotional numbing along with hyperarousal.

PTSD with psychotic symptoms may overlap with categories such as psychogenic psychoses, hysterical psychoses, nonaffective remitting psychoses, acute brief psychoses, reactive psychoses, acute and transient psychoses, and bouffées délirantes. They all refer to psychotic episodes with an acute onset, dramatic symptoms, and relatively rapid resolution, and all show a female preponderance of about seventy-five percent (71-75). The micropsychotic episodes (76) encountered in borderline personality disorder, in which there is a 3:1 preponderance of women (77, 78), should also be included here as they are sometimes confounded with schizophrenia but require different treatment.

Cognitive therapy	Medication
Exposure therapy -- flooding, desensitization	Group treatment
Desensitization and reprocessing	Brief psychodynamic psychotherapy

Conclusions

It has been recently found that, after a year, the diagnosis of nonaffective first-episode psychosis in women shifts away from schizophrenia, whereas in men, it tends to shift toward it (79). This is an indication that, in women, presenting conditions that are not schizophrenia can originally be missed and lead to inappropriate treatment.

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