World Journal of Psychiatry

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DOI: 10.5498/wjp.v4.i4.112

World J Psychiatr 2014 December 22; 4(4): 112-119
ISSN 2220-3206 (online)

REVIEW

Eating disorders and psychosis: Seven hypotheses

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Received: July 16, 2014
Peer-review started: July 16, 2014
First decision: August 28, 2014
Revised: September 16, 2014
Accepted: September 18, 2014
Article in press: September 19, 2014
Published online: December 22, 2014

Abstract

Psychotic disorders and eating disorders sometimes occur in the same person, and sometimes, but not always, at the same time. This can cause diagnostic confusion and uncertainty about treatment. This paper examines seven ways in which symptoms of both conditions can co-exist. The literature on this topic consists to a large extent of case reports, so that firm conclusions cannot be drawn from their examination. There is no consistent sequence in the co-occurrence of the two conditions-eating disorders sometimes precede, and sometimes follow the onset of psychosis. The advent of the psychosis, and sometimes the treatment of the psychosis can cure the eating disorder, but it can sometimes aggravate it. Psychosis is not necessarily a mark of severity in the course of an eating disorder, and food refusal can occur independent of severity in psychotic illness, but it can be a cause of death. There is some genetic association and some overlap of physiologic, cognitive and brain structure deficits in the two types of disorder. The connection between the two, however, remains speculative. The area of comorbidity and overlapping symptoms in psychiatry requires more research. Clinical recommendations include attention to the different individual ways in which these two disparate conditions often overlap.

Key words: Psychosis; Anorexia; Bulimia; Eating disorder; Comorbidity

Core tip: Eating disorder symptoms and psychotic symptoms may co-exist and may serve individual psychological purposes. When planning treatment, the whole person needs to be kept in mind, lest curing one symptom exacerbates another. Effective treatment requires attention to overlapping dimensions of illness.

Seeman MV. Eating disorders and psychosis: Seven hypotheses. *World J Psychiatr* 2014; 4(4): 112-119 Available from: URL: http://www.wjgnet.com/2220-3206/full/v4/i4/112.htm DOI: http://dx.doi.org/10.5498/wjp.v4.i4.112

INTRODUCTION

Working in an outpatient clinic for women with psychotic illness, the author encountered many patients with concurrent problems in eating that made it difficult to decide which symptoms to treat first.

Case example 1

A 25-year-old woman being treated with antipsychotic medication for schizophrenia [Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria] appeared, over a three-month period, to be losing considerable weight. Questions about her eating habits yielded the following answers: "I can't eat much." "The medication upsets my stomach." "If I eat too much, I vomit." On physical exam, her weight was below norms for her height. Heart rate was slowed but regular, and blood pressure was low. Her skin appeared dry.

The treating team entertained the following questions: is the patient suffering only from schizophrenia, or from

an eating disorder as well? Will the eating problems disappear once the psychosis is adequately treated? Should treatment focus more on the eating problems than on the schizophrenia, since self-starvation can lead to acute heart problems and even death, while schizophrenia is a chronic condition?

Case example 2

Another young woman in her mid-twenties who had previously been treated elsewhere for anorexia nervosa (DSM-Ⅳ criteria), developed delusions about being followed and exhibited eccentric public behavior that brought her to the attention of police, and, hence, to the psychosis clinic. Her case raised the following questions among the treating team: could the psychosis be a result of undernutrition? Could the patient be suffering from two separate disorders, anorexia nervosa plus an affective disorder with psychotic features, or possibly schizophrenia? Which of her symptoms should take precedence with respect to treatment?

To help answer the questions of the mental health team, the search terms "eating disorders", "anorexia", and "bulimia" plus "psychosis", "schizophrenia", "delusion" and "hallucination" were entered into the PubMed and Google Scholar databases, with subsequent searching for further references in all relevant articles, many of which turned out to be case descriptions.

Perusal of the literature led to seven potential hypotheses about the comorbidity of psychotic illness (schizophrenia or the presence of delusions or hallucinations in the context of an affective disorder), and eating disturbance. The hypotheses, and the predictions to which they lead, will first be outlined, and subsequently explored in greater detail. Many are contradictory. They are meant only to provoke discussion.

Hypothesis 1: Eating disorders and psychoses are entirely separate disorders that can, by chance, occur in the same person.

Two epidemiologic predictions follow from this hypothesis: (1) The incidence of psychotic disorder among those with eating disorder will be the same as it is in the general population; and (2) The incidence of eating disorder among individuals with psychotic disorder will be the same as it is in the general population.

Hypothesis 2: As a result of starvation, electrolyte, and metabolic imbalance, transient psychotic symptoms can develop in patients with a primary eating disorder. The direction of effects could be in the opposite direction. Patients with a primary psychotic illness (*e.g.*, schizophrenia or delusional depression for instance) can stop eating due to delusions related to food-*e.g.*, the food is poisoned; the food is contaminated, and subsequently develop an eating disorder.

Since the secondary condition depends upon the presence of the first, the prediction here would be that effective treatment of the primary condition would abolish both.

Hypothesis 3: Control of food intake provides a sense of mastery, achievement, and self-control to individuals whose sense of self-efficacy is low, as is the case of individuals at risk for psychosis. Control of food can, thus, be conceptualized as an attempt to ward off acute psychosis. The opposite direction of causality is also possible, namely that apathy, for instance, a negative symptoms of schizophrenia, reduces the urge to purge and diet in anorexia/bulimia-prone individuals.

If hypothesis 3 were true, recovery from one disorder would, in distinction to hypothesis 2, make the other worse.

Hypothesis 4: Because of body image distortions, eating disorders are delusional-*e.g.*, psychotic disorders.

If hypothesis 4 were true, a family history of psychosis should be present in patients with eating disorders, and a family history of eating disorders in patients with schizophrenia and other psychotic illness. The biochemical, cognitive, and anatomical deficits found in one condition should be present in the other. Moreover, as in hypothesis 2 and contrary to hypothesis 3, the successful treatment of one condition would also cure the other.

Hypothesis 5: An eating disorder is an early sign (prodrome) of an impending psychosis or, conversely, psychotic symptoms can herald the beginning of an eating disorder.

If this were the case, one disorder would precede the other and fade into the background once the primary condition surfaced.

Hypothesis 6: Antipsychotics used to treat psychosis lead to weight gain and, thus, induce eating disorder. Conversely, antidepressants used to treat eating disorder can trigger psychosis.

The prediction here is that the second disorder will disappear once the offending treatment is stopped.

Hypothesis 7: Psychotic symptoms are a marker of severity in eating disorders, while food refusal signals a severe and dangerous stage of psychotic illness.

This hypothesis lends itself to two predictions: (1) Patients diagnosed with an eating disorder who exhibit psychotic symptoms will display illness acuity markers-*e.g.*, low body mass index (BMI), electrolyte imbalance, severe depression, high levels of food restriction and purging, suicide attempts, long duration of illness, treatment resistance and a high mortality rate; and (2) Patients diagnosed with a psychotic illness who exhibit food refusal will similarly show markers of illness severity-*e.g.*, poor response to treatment, a large number of psychotic symptoms and signs, frequent hospitalization, involuntary hospitalization, high suicide rate, and a high mortality rate.

TESTING THE HYPOTHESES

Eating disorders and psychoses are entirely separate disorders

Conceptualizing eating disorders and psychotic disorders as falling into two separate, distinct DSM categories is the usual way of thinking about these disorders. The logical extension to acceptance of this belief is that the incidence of psychotic disorders such as schizophrenia for instance, among individuals with eating disorder, reflects their rate in the general population, and the incidence of eating disorders such as anorexia nervosa, for instance, among individuals with psychotic disorder, is on a par with their occurrence in the general population.

Early studies of eating disorder suggested a disproportionally high rate of associated psychotic illness. For instance, in a survey of 1017 eating disorder patients admitted to Danish psychiatric institutions during the period 1968-1986, Møller-Madsen *et al*[1] found that, among those who were rehospitalized during the same time period (which was true for 22%), the diagnosis was changed to psychosis in as many as 6%.

Belief in a disproportionate incidence rate in no longer credible. Once diagnostic criteria were more clearly specified and reliable interview instruments more widely used, the incidence of psychotic illness in the context of eating disorder was shown to be low. In an authoritative review that included 119 separate studies published in the English and German literature prior to 2002 (covering 5590 patients diagnosed with anorexia nervosa), Steinhausen[2] found that a concurrent diagnosis of schizophrenia was, indeed, rare. More recently, Miotto *et al*[3] found no cases of co-morbid schizophrenia among 112 female patients with DSM-IV eating disorders. Schizophrenia was found to be more prevalent, however, among men with eating disorder. Of 98 male veterans with eating disorder, 27 (28%) in one study received a concurrent diagnosis of schizophrenia or other psychosis[4]. This was over three times the rate of psychosis in male veterans who did not have an eating disorder and also over three times the rate of female veterans with eating disorder. One potential explanation for the gender difference is expectation. Clinicians generally do not expect to see eating disorder in men, so that the cognitive distortions and food phobias that accompany eating disorders, while interpreted as overvalued ideas in women, are seen as delusions in men, and therefore considered to indicate psychotic illness.

Although current literature considers full-fledged psychosis to be relatively rare, individual psychotic symptoms are not infrequent in the context of eating disorder. Miotto *et al*[3] found more 'paranoid ideation' and "psychoticism" on the Symptom Checklist-90-Revised[5] symptom checklist in eating disorder patients than in non-psychiatric controls of similar age. Earlier workers[6] had reported that 17 of 130 patients (14%) with eating disorder showed some signs of psychosis. Blinder *et al*[7] however, studying 2436 female inpatients with eating disorder (ED) in 2006, found psychotic symptoms in only 0.4%, (mostly in the restricting anorexia nervosa type of ED), a lesser percentage than the reported rate of psychotic symptoms in the general population[8,9].

Despite these findings, various reviews have reported the incidence of schizophrenia in patients with eating disorders to be between 3%-10%[10] and the incidence of transient psychotic episodes to be 10%-15%[11]. There seems to be no good evidence for such conclusions. Overall, the incidence of psychosis in eating disordered patients is approximately that of the population at large.

Looking at the question the other way around (the incidence of eating disorder in the context of psychosis), Götestam *et al*[12] studied 19000 Norwegian psychiatric patients using a staff report questionnaire and found that, among inpatient males with schizophrenia, 1.71% suffered from eating disorders. The figure was 2.88% for women. When outpatients were included, the percentage came down to 1.6% for males, but rose to 3.8% for females. This suggests that disordered eating occurs much less frequently in association with schizophrenia in men but, in women, more frequently in association with the kind of psychiatric problems (mostly depression and anxiety) found in outpatient clinics. The general population lifetime prevalence of anorexia nervosa, bulimia nervosa, and binge-eating disorder is estimated to be 0.3%, 0.9%, and 1.6% respectively[13]. Considering that community rates of ED are always much higher than rates derived from medical care settings (because most people with ED do not seek medical help), the Götestam *et al*[12] rates of ED in schizophrenia patients are, thus, substantially higher than expected in both men and women.

More recently, Fawzi *et al*[14] in Egypt found that the prevalence of disordered eating [defined by a score of $\geqslant$ 30 on the Eating Attitudes Test (EAT40)[15]] was 30% in 50 antipsychotic-naïve men and women with schizophrenia, compared to 12% in non-psychiatric controls. The patients also had significantly higher EAT40 mean scores than the controls.

The question, therefore, of whether eating disorders and psychotic disorders belong in separate categories of disease and occur together only by chance is unsettled. Perhaps because of help seeking and referral patterns (psychosis being of more clinical concern than ED), patients suffering from both disorders are more in evidence in psychosis services, such as the one to which the two cases described above belonged, than they are in ED services.

Symptoms of eating disorders lead to psychosis, and vice versa

ED patients may suffer from starvation, electrolyte, and metabolic imbalance, conditions that can provoke transient psychotic symptoms. Equally, patients with psychosis may suffer from food-related delusions-*e.g.*, the food is poisoned; the food is contaminated, that lead to food refusal.

If this were the case, one would expect the secondary condition to disappear once the trigger (starvation or

food delusion) were removed.

There are several case reports in the literature of psychosis following starvation caused by anorexia nervosa[16]. Mavrogiorgou *et al*[17] report the case of a 37-year-old woman with anorexia who, for four years, suffered acute paranoid-hallucinatory psychosis at the tail end of fasting episodes. During these four years, psychotic symptoms could not be elicited either before or after the fasting periods, which suggests a cause and effect relationship between the fasting and the psychotic decompensation. The authors hypothesize that the fasting led to acute hyperactivity of the dopaminergic system, giving rise to subsequent psychosis. It has been suggested that starvation is especially psychotogenic when it occurs during adolescence, a critical period for brain structural, neurochemical, and molecular changes[18] that are specifically critical in the regulation of dopamine pathways[19]. Starvation during early adolescence, more than in any other time period, may have a particularly damaging effect on the brain[20]. The duration and severity of starvation-induced psychosis, and ultimately how it is diagnosed and treated, may thus depend on the patient's age at the time of the starvation episodes[21].

On the converse side, patients with schizophrenia develop delusions about food that can subsequently lead to food refusal[22]. What starts as a delusion about food can progress to a condition that meets all the criteria of an ED.

Symptoms of one condition can, thus, act as risk factors for the other condition.

Symptoms of one condition protect against the other condition

The prediction here is opposite to that of hypothesis 2. Control of food intake provides a sense of mastery, achievement, and self-control to individuals who may be at risk for psychosis. The increase in feelings of self-efficacy can then help to ward off the psychosis. It is also possible that a symptom of psychosis, such as apathy for instance, can ward off an eating disorder.

If this were the case, then, in some individuals, recovery from ED would precipitate psychosis and recovery from psychosis would trigger an ED.

Deckelman *et al*[23] present four cases where schizophrenia and bulimia coexist and where the negative symptoms of schizophrenia appear to diminish the drive to restrict eating or the impulse to binge and purge. There are also case reports of psychosis that first manifests after a person has recovered from an ED[24]. Case reports are, of course, not evidence for or against a hypothesis. They merely demonstrate that reciprocal relationships, such as the ones described above, can and do occur. They were first suggested by David *et al*[25] and illustrated by a clinical case in which EAT40 scores[15] rose when psychosis was contained and declined when psychosis was at its peak. Hugo *et al*[26] presented four cases that showed the same reciprocal relationship. They argued that disordered eating can be used as a defense against a more fragile, disintegrated state such as psychosis. Yet again, in a review of male cases, Bou Khalil *et al*[27] conclude that, in general, symptoms of ED diminish when psychotic episodes flare and recur when psychotic episodes go into remission.

It is interesting to speculate why this reciprocal relationship might make sense. The pre-psychotic state is often accompanied by a distorted sense of agency and a loss of control[28,29] that can be initially counteracted by exerting control over eating. For example, Yamashita *et al*[30] reported the case of a 14-year-old girl whose anorexia nervosa, present for about two years, abruptly shifted after two weeks of hospitalization to an acute psychosis characterized by persecutory delusions and auditory hallucinations. All traces of the eating disorder disappeared, as if control over eating no longer served a purpose. Rojo-Moreno *et al*[31] recently reported two cases that followed a similar trajectory. There are several potential interpretations of these cases. The ED might protect against psychosis. It could also be argued that the ED was a prodrome of psychosis. Another possibility is that the antipsychotics used to treat the psychosis also cured the ED[32-35].

Eating disorders and psychotic disorders are marked by similar cognitive distortions, perceptual defects, genetic markers, physiologic and anatomical abnormalities

It can be argued that eating disorder and psychotic disorder are different expressions of the same illness, the distorted thoughts about eating being a form of delusion[36] (Mountjoy). Interestingly, auditory hallucinations, the hallmark of psychotic conditions, also occur in anorexia nervosa[23,31,37,38]. Depersonalization and derealization, too, are common symptoms of both disorders[11], as are overvalued ideas[39,40].

If the two conditions were different aspects of the same illness, family medical history should be positive for both disorders and successful treatment of one condition should cure the other as well. In addition, biochemical, cognitive, and anatomical deficits found in one condition should also be present in the other.

Data from the National Survey of American Life show an association between having a first-degree relative with schizophrenia and the lifetime development of bulimia, among other disorders[41]. Among other possibilities, this association could be the result of shared genes. The genetics of ED was recently reviewed by Trace *et al*[42]. They found that dopamine receptor D2 polymorphisms were significantly associated with anorexia nervosa, as they have been in genome-wide association studies in schizophrenia[43]. Significant associations have been shown between the Val158Met polymorphism of the catechol-O-methyl transferase gene and anorexia nervosa, and schizophrenia[44]. It is not unusual in modern psychiatric genetics to find that risk genes cross traditional diagnostic boundaries[45], suggesting the importance of epigenetic factors in the determination of specific psychiatric syndromes. In both ED and psychotic disorders, dopamine genes have been found to be dysregulated as a result of epigenetic influences[46].

With respect to treatment response, Wenokur *et al*[38]

present a case where an eating disorder and a psychotic disorder disappeared together in response to one treatment. Patients with ED co-morbid with psychosis have been reported to do well on drugs that act on the dopaminergic system[47,48]. Both disorders have been linked to altered dopamine activity, manifested in anorexia nervosa mainly by hyperactivity[49,50] and, in psychotic illness, mainly by delusions and hallucinations. Altered dopamine activity in ED is present even after recovery, suggesting that it is more than a sequela of undernutrition[51].

Many brain alterations are associated with anorexia nervosa and tend to be distributed across the same brain structures implicated in schizophrenia[52]. Studies have found abnormal functioning in ED in the frontal, limbic, occipital, striatal and cerebellar regions, deficits that sometimes persist after the patient has recovered, which suggests that the dysfunction is not merely a consequence of poor nutrition[53].

Many of the cognitive and social dysfunctions found in ED are reminiscent of those seen in psychotic disorders. A basic lack of trust leading to social isolation, poor therapeutic alliance, and poor treatment adherence is common to both disorders[54,55]. The ability to put oneself in the mindset of the other person (theory of mind) is deficient in both disorders[56], as are difficulties in shifting sets or rapidly being able to pass from one mode of thinking to another[57]. Similarity in these dimensions of illness is not, of course, limited to eating disorders and psychotic disorders.

While most of the work in these areas is new, the idea that ED and schizophrenia patients suffer from similar cognitive impairment had been suggested earlier by Yamashita *et al*[30].

The symptoms of one disorder can herald the onset of the other disorder

An ED can be the early sign of an impending psychosis, or psychotic symptoms can signal the beginning of an ED.

If such were the case, one disorder would precede the other and disappear when the other emerged.

Historically, at the beginning of the 20th century, French psychiatrists considered anorexia nervosa to be a prodrome for schizophrenia[58], and this idea subsequently entered British psychiatry[59,60]. As recently as 2013, a study of 11067 youth found that those who later developed a psychotic disorder (n = 21) had reported more ED symptoms at age 16 than those who remained free of psychosis[61].

The case against eating symptoms serving exclusively as a prelude to psychosis is made by case reports illustrating the fact that ED sometimes arises in the midst of an existing psychotic illness[10,17,21,62]. Even when ED does start first, in these cases it does not go away when psychosis appears, so it cannot be considered a prodrome. Sometimes, eating disorders occur very late in the course of schizophrenia. Stein *et al*[63] describe four elderly patients suffering from a chronic form of schizophrenia who, for the first time, developed eating disorders late in life. The schizophrenia, however, did not disappear when the ED emerged.

Erin Hawkes, who suffers from schizophrenia and has written an insightful book about her experience with this illness[64], writes about bulimia as a response to schizophrenia symptoms. The order of onset of eating disorder *vs* psychosis in those who eventually suffer from both conditions is so variable that neither can justifiably be considered a prodrome of the other. Shiraishi *et al*[65] convincingly illustrated this variability by graphing their eight cases.

The treatment of one disorder is responsible for the onset of the other

Antipsychotics used to treat psychosis instigate weight gain that subsequently induces eating disorder. By the same token, antidepressants used to treat eating disorders can precipitate psychosis.

If this were the case, the second disorder would disappear once treatment for the first were stopped.

Hawkes[66] writes that her bulimia worsened after treatment with olanzapine: "I was put on olanzapine. Terrible mistake: I was, within two months, 137 pounds of (in my opinion) fat. My purging went wild…. Olanzapine gave me a ravenous appetite…. Thus, purging became all-important".

There have been several reports of medication-induced bingeing resulting from treatment of eating disorder with antipsychotic agents[67-71]. A 2013 meta-analysis of 8 randomized trials of the use of the newer antipsychotic agents (six olanzapine, one risperidone, one amisulpride) for eating disorders concludes that, compared with placebo, their use was associated with a nonsignificant increase in BMI that exerted a nonsignificant effect on the drive for thinness and on body dissatisfaction[72], in other words, affording no reason to believe that treatment with antipsychotics worsened eating disorders. The doses prescribed were relatively low, however, (4.2 mg-10 mg for olanzapine), lower than would have been prescribed had the target been psychosis. The other potential explanation for the negative finding is that only two of the eight studies covered in the meta-analysis controlled for medication adherence. Many of the patients may not have taken their prescribed doses. The jury is still out, therefore, on the possibility that antipsychotic treatment can induce eating disorder.

With respect to treatments for ED that might precipitate psychosis, antidepressants, often used in the treatment of eating disorders, are known to sometimes result in psychosis[73,74].

Psychosis may be a severity marker in eating disorder. Conversely, not eating may be a severity marker for psychotic illness

If that were the case, then ED patients with psychotic symptoms might be more severely ill than other ED patients along a number of parameters such as duration of illness, treatment resistance and mortality rate. By the same token, food refusal could be a marker of severity in

psychosis patients. If so, it would be associated with non-response to treatment and a high mortality rate.

Other than the acknowledgement that three domains need to be considered to ascertain severity in ED-the psychological (*e.g.*, depression), the behavioral (*e.g.*, eating and purging behaviors), and the physical (*e.g.*, BMI; hyperactivity; electrolyte imbalance), there is no agreed upon severity scale for these disorders[75]. Early on, Lasegue[76] delineated three phases of "hysterical anorexia" as he called it, the first marked by an "uneasiness and fullness" after eating, with consequent reductions in food intake, the second marked by severe restriction, increased activity levels and an "intellectual perversion" resulting in a complete denial of the illness, and the third marked by "extreme emaciation, laborious exercise and general debility"[77]. Currently, the markers of severity are usually BMI, physical risk, and illness duration (not psychosis)[78]. The literature does not support a correlation of psychosis with severity in ED.

Nor is there any evidence to suggest that food refusal in the context of psychosis is an indicator of severity of psychotic illness, although not eating can aggravate psychotic symptoms[79,80] and, if left untreated, lead to death by starvation.

Both ED and psychotic disorders have a high mortality rate from suicide, substance abuse and medical complications. In ED, cardiovascular complications arise from malnutrition, dehydration, and electrolyte abnormalities, precipitating death by inducing heart failure or fatal arrhythmias. In psychotic disorders, the cardiovascular system is compromised by obesity and the metabolic complications of antipsychotic drugs[81-83]. Deliberate starvation can lead to death in persons with long standing psychosis but is not generally viewed as a marker of severity in psychotic illness.

CONCLUSION

The combination of eating disorder and psychotic illness is more often seen in services for psychotic disorders than in eating disorder services, probably because psychotic symptoms take precedence in terms of referral. The "doubly disordered" risk being undertreated in schizophrenia services because the ED may appear trivial in comparison to the more flagrant psychotic symptoms and may worsen insidiously due to the effects of weight gain induced by antipsychotic medication. Clinicians need to be aware of the fact that, because of undernutrition, ED can precipitate a state that looks like psychosis, but that is usually transient. During adolescence, however, when the developing brain is exquisitely vulnerable to insult, acute starvation may kindle a psychosis that takes on a life of its own. It is also the case that the delusions of a primary psychotic condition can lead to food aversions and initiate dangerous eating behavior. Some have argued that ED symptoms can protect against the development of psychosis and psychotic symptoms can protect against ED. This may be true for some individuals, and clinicians need to be alert to this possibility. Some dimensions of illness are common to both conditions and research in this area is accelerating. Also clinically interesting is the phenomenon of eating disorders serving as a prodrome or early stage of psychosis, and eating disorders emerging as a result of the treatment of psychosis. Reports of such cases have been relatively prevalent; phenomena of this sort need to be documented and better studied.

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P- Reviewer: Cocchi A, Serafini G, Thomas JJ
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