**Name of Journal:** *World Journal of Psychiatry*

**Manuscript NO:** 74241

**Manuscript Type:** MINIREVIEWS

**Differences between delusional disorder and schizophrenia: A mini narrative review**

González-Rodríguez A *et al*. Differences among psychoses

Alexandre González-Rodríguez, Mary V Seeman

**Alexandre González-Rodríguez,** Department of Mental Health, Mutua Terrassa University Hospital, University of Barcelona, Barcelona 08280, Spain

**Mary V Seeman,** Department of Psychiatry, University of Toronto, Toronto M5P 3L6, Ontario, Canada

**Author contributions:** Gonzàlez-Rodriguez A conceived the idea of writing this review, based on our joint clinical experience treating patients with delusional disorder and schizophrenia; both authors contributed equally to decisions about the method and the content; both authors contributed equally to the literature search, and to decisions about what studies to include; both authors shared in the clinical contributions; there were several drafts; Seeman MV perfected the final version.

**Corresponding author: Mary V Seeman, DSc, MDCM, OC, Professor Emerita,** Department of Psychiatry, University of Toronto, #605 260 Heath St. West, Toronto M5P 3L6, Ontario, Canada. mary.seeman@utoronto.ca

**Received:** December 18, 2021

**Revised:** March 23, 2022

**Accepted:** April 21, 2022

**Published online:** May 19, 2022

**Abstract**

Psychotic syndromes are divided into affective and non-affective forms. Even among the non-affective forms, substantial differences exist. The aim of this relatively brief review is to synthesize what is known about the differences between two non-affective psychoses, schizophrenia and delusional disorder (DD), with respect to clinical, epidemiological, sociodemographic, and treatment response characteristics. A PubMed literature search revealed the following: in schizophrenia, hallucinations, negative symptoms and cognitive symptoms are prominent. They are rare in DD. Compared to schizophrenia patients, individuals with DD maintain relatively good function, and their delusions are believable; many are beliefs that are widely held in the general population. Treatments are generally similar in these two forms of psychosis, with the exception that antidepressants are used more frequently in DD and, for acute treatment, effective antipsychotic doses are lower in DD than in schizophrenia. It is with the hope that the contrasts between these two conditions will aid in the provision of safe and effective treatment for both that this review has been conducted.

**Key Words:** Non-affective psychosis; Delusional disorder; Schizophrenia; Epidemiology; Symptoms; Treatment response

**©The** **Author(s) 2022.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation:** González-Rodríguez A, Seeman MV. Differences between delusional disorder and schizophrenia: A mini narrative review. *World J Psychiatry* 2022; 12(5): 683-692

**URL:** <https://www.wjgnet.com/2220-3206/full/v12/i5/683.htm>

**DOI:** https://dx.doi.org/10.5498/wjp.v12.i5.683

**Core Tip:** Although patients with delusional disorder and schizophrenia share clinical similarities, epidemiological and treatment outcomes suggest that these two conditions belong to different diagnostic categories. The onset of delusional disorder (DD) occurs at a relatively late age and, in contrast to schizophrenia, everyday functioning is preserved. Treatment is similar, with more frequent use of antidepressants in DD. Effective targeting of symptomatic domains is important in both these forms of psychosis.

**INTRODUCTION**

Schizophrenia and delusional disorder (DD) are both non-affective psychoses and symptoms overlap in many ways. Both conditions are characterized by the presence of delusions although, in schizophrenia, hallucinations, cognitive deficits, and features such as thought disorder, apathy, and social isolation are as much in evidence as are delusions. In both disorders, delusions are usually centered around themes of persecution, but grandiosity, morbid jealousy, erotomania, and delusionally interpreted somatic sensations are also very common[1] (Table 1). According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), delusions, in whatever psychotic illness they are found, are defined as fixed beliefs that are not easily amenable to correction, despite proof to the contrary.

Although Table 1 represents the current sub-classification of DD, several investigators have attempted to introduce different groupings within this diagnostic category. Wustmann and collaborators[2] classified DD patients into three groups: erotocentric (erotomanic delusions and delusions of jealousy), somatocentric (delusions of health threat and somatic delusions) and securocentric (persecutory, querulous, litigious delusions, and delusions of reference). Some patients present with two or more different types of delusion over time. In the schizophrenia literature, although some contemporary writers still refer to paranoid schizophrenia as a subtype, sub-grouping according to delusional content is largely obsolete.

The aim of this brief narrative review is to search the existing psychiatric literature in order to address the following questions: (1) Do epidemiological data differentiate DD from schizophrenia? (2) Do clinical features or psychiatric comorbidities differ in DD and schizophrenia? And (3) Are there data that show differences between DD and schizophrenia with respect to response to treatment, both pharmacological and psychosocial?

**Theoretical speculations on the origin of delusions**

How delusions take root and grow in a human mind is a much-debated topic, which, it is agreed, results from the interaction of biological, psychological and environmental factors.

Theorists believe that delusions arise from chance exposure to an event that feels special, out of the ordinary[3]. A preoccupation with “how could this possibly have happened to me?” begins to torment the individual until a ‘eureka’ moment is reached when everything falls into place[4]. This has been called the “aha” experience[5] when an explanation, sometimes seemingly outlandish, has at last been found.

Despite the fact that the eureka explanation sounds, when shared, implausible to others, it can germinate and plant itself firmly in the mind of a biologically vulnerable individual and become a quasi-permanent, salient feature in that person’s life[6]. Family members and friends question the explanation, argue against it, which frequently leads to conflicts that culminate in the social isolation of the deluded person[7]. To account for this process in the context of schizophrenia, most of the literature assumes a genetic predisposition inherent in the deluded person; in DD, on the other hand, because delusions emerge later in life, they are often attributed to acquired brain pathology[7]. In both conditions, biological underpinnings that make the ground fertile to delusions are assumed, but clear evidence of brain structure/function impairment is usually lacking[8].

Psychological origin theories are not excluded[9,10], especially not in DD. Formative traumatic experiences are thought to lead to negative emotions such as shame, guilt, or fear, resulting in a “be on your guard” attitude that transforms ordinary events into threats that grow to become convictions of deliberate persecution[11]. Some have argued that emotionally aroused states facilitate hypervigilance to threat, and that such states of mind lead to both misinterpretations and, especially in schizophrenia, misperceptions[12].

It is possible that phenomena such as these arise frequently in many people but are then aborted by feedback from trusted others. Individuals who are socially isolated may not have access to such feedback. It is also possible that, occasionally, delusional explanations for extraordinary events persist because they are reinforced by external affirmation[13].

There is a school of thought that attributes the persistence of a delusion not only to outside reinforcement but also to the susceptible person’s habitual form of reasoning, or cognitive biases. Such biases have biological underpinnings but may also represent learned phenomena. One example of a cognitive bias is the tendency to jump too quickly to unwarranted conclusions[14]. As described by Laukkonen *et al*[4], the more that a person comes to faulty conclusions about everyday events, the more ‘proofs of concept’ are incorporated into an ever-expanding delusional system. It is psychologically easy to attribute mistakes and disappointments to perceived foes and conspirators[15]. Gunn and Bortolotti[16] note that paranoid delusions, by placing blame for missteps on outside persecutors, serve as ‘secondary gain,’ allaying the guilt and shame of personal failings. In cultural anthropology, an important distinction has been made between guilt cultures, shame cultures, and cultures of fear[17], classified on the basis of traditionally preferred ways by which parents socialize their children. In this context, Matos *et al*[18] speak of shame memories as central to the development of paranoia. Carvalho *et al*[19] emphasize instead the influence of family narratives and childhood memories on the emergence of paranoid ideation. In a much-cited paper, Kirmayer and Ryder[20] conclude that cultural habits are embedded in the brain as neural correlates of emotion[21], and can thus predispose to different forms of mental symptoms in different cultures.

The literature continues to leave the issue of the origin of delusions open. It is possible, however, to arrive at a conclusion that delusional thinking in psychoses that begin at older ages (such as DD) is likely to originate mainly in life experiences whereas delusions that begin in youth (as in schizophrenia) are rooted in neurodevelopment, with most current research centered on aberrations of neurotransmission, especially dopamine transmission[22-24]. A recent positron emission tomography study found dopamine dysregulation in both schizophrenia and DD[25]. This suggests a neurocognitive model for delusion formation that links aberrant salience of a chance stimulus, often threat-related, with mesostriatal dopamine signaling. Secondary cognitive processes are recruited to try to make sense of what is perceived as a highly unusual, highly significant experience. These processes, namely jumping to conclusions, unswerving attachment to one’s original conclusions, and inattention to counterarguments, for which dopamine dysregulation may also be responsible, maintain and sustain the delusion[26]. This is a model of delusion formation that also leaves room for a major contributory role for prior experience of trauma and sociocultural input[27].

**Epidemiology**

The lifetime prevalence of schizophrenia, despite variations in study design, geographic source, and study quality, is estimated at 0.48%-1%[28]. This isin contrast to the lifetime prevalence of DD, rated as 0.2%[1], but reported by some researchers to be a decimal place rarer - 24 to 30 per 100000[29]. Prevalence varies with the characteristics of the study sample and the setting of the investigation[30].

A major difference between schizophrenia and DD is the age of onset, late teens and early adulthood in schizophrenia, middle age and above in DD[30]. Onset age is critical in many ways. For example, the fact that DD first occurs, for the large part, in postmenopausal women may explain why gender differences during the reproductive years are not as marked in this disorder as they are in schizophrenia, where circulating estrogen levels protect the brains of reproductive age women[30,31]. Onset age may also affect the thematic content of delusions. In DD, erotomania, for instance, has been found to be more frequent in women with premenopausal onset while somatic and jealous delusions are more common in women whose onset is postmenopausal[32].

Epidemiological differences between DD and schizophrenia depend to a significant degree on the diagnostic instrument and the diagnostic criteria and the specific syndromes that are included under the two categories. Some syndromes within the schizophrenia spectrum, such as paranoia querulans (incessant legal actions to obtain compensation for perceived wrongs) and paraphrenia (psychotic symptoms first diagnosed in the elderly) have been removed from current classification systems and are now subsumed under either DD or schizophrenia. This is notably the case for paraphrenia, which is now variably categorized as late onset schizophrenia, atypical psychosis, schizoaffective disorder or DD[33]. Shifts such as these in diagnostic labeling contribute to changes in reported prevalence of the two disorders.

With respect to the prevalence of subtypes, most investigations agree that persecutory delusions are the most common in both conditions[34], followed, in DD, by jealous, somatic and erotomanic delusions[32,35].

In contrast to schizophrenia which, in addition to delusions, comes with prominent hallucinations, negative, and cognitive symptoms, DD is usually considered a disorder of delusions only. Phenotypic factorial analyses of DD, however, have identified 4 independent symptom areas: delusions, hallucinations, depression, and irritability[36]. This suggests that DD, as diagnosed today, is symptomatically heterogeneous, with symptoms that overlap to a considerable degree with those of schizophrenia. de Portugal and co-workers[37], who also investigated this question, found 4 symptom categories in DD, paranoid, cognitive, schizoid and affective, which, together, explained 59% of the variance in symptomatology.

In clinical practice, both schizophrenia and DD patients frequently present with psychiatric comorbidities, mainly affective disorders. In DD, depressive disorders have been found in 21%-55.8% of patients[38]. Women may present with more mood symptoms than men, but findings in this area are controversial[2,35]. In schizophrenia, it has been noted that delusional themes can change over time in approximately one-third of cases[39]. In terms of functional ability, patients with DD show a significantly superior global functioning than patients with schizophrenia, suggesting that DD is distinct from schizophrenia, and, on the whole, less severe[40].

**Clinical approach to patients with delusions**

The literature strongly suggests that, when beginning treatment with a person who is delusional, whatever the specific diagnosis, the first concern must be safety - safety for the patient, for persons who the patient believes are enemies and for family members and treating personnel who may become incorporated into the patient’s delusional system. Suicide is a risk because low self-esteem often lies at the core of delusions. Adding to the concern for safety is the fact that, depending on a jurisdiction’s mental health legislation, involuntary treatment can be difficult for the family to arrange, even in situations of imminent danger[41].

Once safety concerns have been allayed, the next challenge is to build a therapeutic alliance by patient and clinician working together toward common goals[42].Clinical practice suggests that initial goals need not be ambitious but must have patient buy-in. For instance, because delusions take their toll on sleep quality, working together to improve sleep by using sleep hygiene techniques and sedatives is likely to engage initially treatment-resistant patients[43].

Succeeding at something together builds trust and paves the way to information-sharing and, ultimately, to discussion of sensitive topics such as the objective veracity of a delusional belief. But this can wait[44]. Experienced clinicians always acknowledge the subjective veracity of the belief.

When engaging patients who have difficulty with trust, many therapists recommend starting by discussing early childhood because patients are less likely to perceive past issues as threatening compared to the potential threat of the therapist dismissing their accounts of current history[45]. Whereas experience and skill are always clinically useful, there is a consensus that a therapist’s genuineness is the most important ingredient in forging a trusting therapeutic bond[46].

Ongoing therapy largely consists of enhancing the patient’s self-esteem, bolstering resilience and improving metacognitive skills[47]. Judiciously planting seeds of doubt about the reality of a delusion by exploring alternate explanations is a key metacognitive technique[48]. Cognitive-behavioral techniques have successfully eliminated delusional ruminations, negative beliefs about the self, interpersonal oversensitivity, as well as sleep disturbance, each of which has been shown capable of reinforcing delusions[49].

Techniques recommended for delusional jealousy consist of targeting common tendencies found in such patients, *e.g.,* inferring the emotions and intentions of others, personalizing chance occurrences, overgeneralizing from one or two experiences, and persistently anticipating catastrophe[50]. Other therapeutic targets are hypervigilance, negative self-esteem, and the inclination to mistrust others. Reframing a patient’s view of a situation is an important therapeutic technique[51] *e.g.,* “He does go out a lot, but it might be because you give him a hard time at home rather than because he’s seeing another woman.” Experienced clinicians believe that therapists do well to embrace the role of educator, teaching patients about emotions and the many ways in which strong feelings can drive behavior[52]. Practice sessions and homework assignments relevant to the expression of emotions are cited as a vital part of cognitive therapy and rehabilitation protocols for all forms of delusions[53].

These recommendations apply to the initial approach to patients with both DD and schizophrenia, but are less effective when the patient’s cognition is impaired. Table 2 summarizes the main recommendations for an initial approach to DD.

**Pharmacological treatment**

Definitions of response to antipsychotic or other pharmacological treatment vary. Response criteria based on reduction in standard rating scale scores, as is done in schizophrenia[54], have been recommended in DD[55] where, thus far, response has been defined on the basis of clinical opinion.

The most recent study in this area was an observational registry- based cohort study in a Swedish population diagnosed with DD[56]. Hospitalization and work disability were found to be less likely occurrences when antipsychotic were prescribed, compared to when they were not. Protection was best conferred by clozapine, olanzapine and all long-acting injectable antipsychotics. When comparisons were made between DD and schizophrenia, a relatively smaller dose of haloperidol (4.7 mg/d) was effective in suppressing delusional symptoms in DD than in schizophrenia (12.7 mg/d)[57]. Treatment was shorter (65 d) in DD compared to 104 d in schizophrenia. At hospital discharge, the global assessment of functioning score was also significantly higher in DD[57]. Although more studies are needed, this suggests that an acute episode of DD may respond to treatment at lower doses and within a shorter time period than an acute episode of schizophrenia. Studies on comparative longer-term response to antipsychotics are, however, lacking.

***Factors influencing drug response***

Adherence to prescribed drug regimens is generally acknowledged as a critical factor influencing therapeutic response. In turn, adherence is influenced by the patient’s gender, age, duration of illness, comorbidities, number of concomitantly prescribed drugs, simplicity of the drug regimen, and quality of the therapeutic relationship[2,58]. Thomas and colleagues[59] have studied these factors as they pertain to schizophrenia, but this has not yet been done in DD.

Specific host genes may enhance or diminish drug response. Morimoto *et al*[57] investigated the relationship between variants of dopamine receptor genes and the tyrosine hydroxylase gene in DD patients, schizophrenia patients, and healthy controls. They found an association between genetic variability in DRD3 and plasma homovannilic acid (pHVA). Specifically, patients with DD homozygous for the DRD3 gene Ser9Ser showed higher pretreatment levels of pHVA than others, an effect especially marked, in this sample, among patients with the persecutory subtype of DD. Aided by structural and functional neuroimaging, work on the genetics of drug response in DD and schizophrenia is underway.

A multicenter positron emission tomography and magnetic resonance spectroscopy study (STRATA) tested whether striatal dopamine synthesis capacity and/or elevated anterior cingulate cortex glutamate levels can differentiate between patients with psychosis who do and do not respond to antipsychotic medications[60]. The findings revealed a potential role of glutamate levels (but not striatal dopamine synthesis) in the prediction of response.

Very few studies have investigated the biological basis of treatment response in DD. In the case of the delusional infestation subtype of DD, one study, however, identified distinct patterns of prefrontal, temporal, parietal, insular, thalamic and striatal dysfunction implicated in response[61].

Therapeutic drug monitoring is currently a promising technique that can evaluate treatment efficacy, correlate adverse events to prescribed doses and assess adherence. While it is often used in the treatment of schizophrenia, it is still rarely done when treating DD patients.

***Use of antidepressants***

Antidepressants have been used as monotherapy in DD when clinicians believe that the delusion is caused by depression. Paroxetine and clomipramine are examples of antidepressants commonly used[62]. Antidepressants used as an adjunct to antipsychotics is a frequent treatment strategy in both DD and schizophrenia.

**Non-pharmacological treatments**

Cognitive therapy has been shown to be helpful in DD[63], as it is in schizophrenia[64,65]. Patients receiving CBT show a significant reduction in the strength of their delusional conviction, in the intensity of the affect associated with their delusion, and in the frequency of behaviors resulting from their delusion.

Table 3 presents the main pharmacological and psychosocial interventions used in the management of patients with DD and schizophrenia.

**Risk of suicide**

Neither suicide antecedents nor suicide rates have, to date, been compared in DD and schizophrenia. Existing studies have established the percentage of suicidal behavior in patients with DD to be between 8% and 21%[66]. In schizophrenia, it hovers around 10%[67]. In both disorders, men are more at risk for completing suicide than women[38]. The somatic subtype and the persecutory subtype of DD are most associated with suicide[30] whereas, in schizophrenia, suicide appears to depend not on delusional theme but on the presence of command hallucinations[68].

**Discussion**

When we began our review, we wanted to address 3 questions: (1) Do epidemiological data differentiate DD from schizophrenia? (2) Do clinical features or psychiatric comorbidities differ in DD and schizophrenia? And (3) Are there data that show differences between DD and schizophrenia with respect to treatment response to either pharmacological or non-pharmacological treatment?

We found an overlap between the diagnosis of DD and schizophrenia, with boundaries often very blurred. As characterized in DSM-5, the middle age onset of DD distinguishes it from the earlier onset in schizophrenia. The literature gives a prototypical picture of schizophrenia as one of hallucinations, cognitive, and negative symptoms in addition to delusions, with function deteriorating over time. Relatively good function is maintained in DD. While this disorder is also characterized by symptoms other than delusions (mainly affective symptoms), delusions predominate. Treatment response to antipsychotic medication appears to be similar in the two conditions, although DD patients, as a group, are older, and would be expected, as one study has shown, to require comparatively lower doses to achieve symptom reduction. When compared to younger age, older age, however, can limit the benefits of pharmacotherapy because of an increased frequency of potential drug interactions and adverse events. An adequate long term comparison of drug response in the two conditions is lacking. Clinical reports recommend the addition of antidepressants to the medication regimen of patients with DD, but large-scale trials to prove the usefulness of this strategy have not yet been conducted. Specific symptoms, when targeted by cognitive behavioral therapies, respond in both DD and schizophrenia, although efficacy trials in DD are, to date, limited.

The content of delusions seems more understandable in DD than it often is in schizophrenia but the major theme is one of persecution in both conditions. In general, the prevalence rate for delusional disorder is significantly lower than that for schizophrenia.

Importantly, a persecutory delusion is such a firmly held belief that it can often lead to behavior which endangers the believer and the persons implicated in the delusion. Safety is a paramount concern; suicide is an important risk. Evidence for the success of current interventions into prevention of suicide and aggression remains relatively weak.

There are many limitations to this narrative review. There is an extremely large literature on schizophrenia, with well-controlled randomized trials of treatment options. This does not yet exist for delusional disorders. Because of the symptom overlap and the prevalence disparity as well as the age discrepancy, well-defined comparative groups are difficult to recruit. Much of the literature on delusional disorders consists of small case series or reports of individual cases. To accurately answer the questions posed in this review, methodologically well-conducted, multicenter trials are required. The review should nonetheless be helpful for clinicians, especially with respect to initial approaches to patients with delusions, and the cautions about safety.

**CONCLUSION**

This brief review covers the recent literature on difference between two non-affective psychoses, DD and schizophrenia. The former is much rarer and presents at older ages. More often than schizophrenia, DD is accompanied by depression, which increases the risk for suicide. Acting out against imagined persecutors is a potential danger in both disorders. While delusions are prominent in both schizophrenia and DD, other psychiatric symptoms may also be present and may require targeted treatment. In contrast to schizophrenia, outside the sphere of the delusion, cognitive functions are usually not impaired in DD, so that a therapeutic alliance is possible and is essential for treatment to succeed. Research into the efficacy of specific treatments is, however, sparse in DD.

This review covers what is known and not known about similarities and differences between schizophrenia and DD, with the hope that highlighting contrasts between these two overlapping conditions will ultimately improve the treatment of both. Future research must address the difficult task of designing rigorous clinical trials that compare response to therapeutic interventions for delusions in individuals whose primary diagnoses may vary.

**REFERENCES**

1 **American Psychiatric Association**. Diagnostic and Statistical Manual of Mental Disorders (DSM-5). 5th ed. Arlington (US): American Psychiatric Association 2013 [DOI: 10.1176/appi.books.9780890425596]

2 **Wustmann T**, Pillmann F, Marneros A. Gender-related features of persistent delusional disorders. *Eur Arch Psychiatry Clin Neurosci* 2011; **261**: 29-36 [PMID: 20700601 DOI: 10.1007/s00406-010-0130-1]

3 **Bortolotti L**. Delusion. In: Zalta EN. The Stanford Encyclopedia of Philosophy, 2008. Available from: https://plato.stanford.edu/archives/spr2018/entries/delusion/

4 **Laukkonen RE**, Kaveladze BT, Tangen JM, Schooler JW. The dark side of Eureka: Artificially induced Aha moments make facts feel true. *Cognition* 2020; **196**: 104122 [PMID: 31759277 DOI: 10.1016/j.cognition.2019.104122]

5 **Sips R**, Van Duppen Z, Kasanova A, De Thurah L, Texeira A, Feyaerts J, Myin-Germeys I. Psychosis as a dialectic aha- and anti-aha-experiences: a qualitative study. *Psychosis* 2020; **13**: 47-57 [DOI: 10.1080/17522439.2020.1798492]

6 **McKay RT**, Dennett DC. The evolution of misbelief. *Behav Brain Sci* 2009; **32**: 493-510; discussion 510-561 [PMID: 20105353 DOI: 10.1017/S0140525X09990975]

7 **Kendler KS**. The Clinical Features of Paranoia in the 20th Century and Their Representation in Diagnostic Criteria From DSM-III Through DSM-5. *Schizophr Bull* 2017; **43**: 332-343 [PMID: 28003468 DOI: 10.1093/schbul/sbw161]

8 **Vicens V**, Radua J, Salvador R, Anguera-Camós M, Canales-Rodríguez EJ, Sarró S, Maristany T, McKenna PJ, Pomarol-Clotet E. Structural and functional brain changes in delusional disorder. *Br J Psychiatry* 2016; **208**: 153-159 [PMID: 26382955 DOI: 10.1192/bjp.bp.114.159087]

9 **Catone G**, Gritti A, Russo K, Santangelo P, Iuliano R, Bravaccio C, Pisano S. Details of the Contents of Paranoid Thoughts in Help-Seeking Adolescents with Psychotic-Like Experiences and Continuity with Bullying and Victimization: A Pilot Study. *Behav Sci (Basel)* 2020; **10**: 122 [PMID: 32751057 DOI: 10.3390/bs10080122]

10 **Rauschenberg C**, van Os J, Goedhart M, Schieveld JNM, Reininghaus U. Bullying victimization and stress sensitivity in help-seeking youth: findings from an experience sampling study. *Eur Child Adolesc Psychiatry* 2021; **30**: 591-605 [PMID: 32405792 DOI: 10.1007/s00787-020-01540-5]

11 **Smurzyńska A**. The role of emotions in delusion formation. *Stud Log Gramm Rhetor* 2016; **48**: 253-263 [DOI: 10.1515/slgr-2016-0066]

12 **Fuentenebro F**, Berrios GE. The predelusional state: a conceptual history. *Compr Psychiatry* 1995; **36**: 251-259 [PMID: 7554868 DOI: 10.1016/s0010-440x(95)90069-1]

13 **Corlett PR**, Krystal JH, Taylor JR, Fletcher PC. Why do delusions persist? *Front Hum Neurosci* 2009; **3**: 12 [PMID: 19636384 DOI: 10.3389/neuro.09.012.2009]

14 **Rauschenberg C**, Reininghaus U, Ten Have M, de Graaf R, van Dorsselaer S, Simons CJP, Gunther N, Henquet C, Pries LK, Guloksuz S, Bak M, van Os J. The jumping to conclusions reasoning bias as a cognitive factor contributing to psychosis progression and persistence: findings from NEMESIS-2. *Psychol Med* 2021; **51**: 1696-1703 [PMID: 32174291 DOI: 10.1017/S0033291720000446]

15 **Lancellotta E**, Bortolotti L. Are clinical delusions adaptive? *Wiley Interdiscip Rev Cogn Sci* 2019; **10**: e1502 [PMID: 31056862 DOI: 10.1002/wcs.1502]

16 **Gunn R**, Bortolotti L. Can delusions play a protective role? *Phenomenol Cogn Sci* 2018; **17**: 813-833 [DOI: 10.1007/s11097-017-9555-6]

17 **Creighton MR**. Revisiting shame and guilt cultures A forty-year pilgrimage. *Ethos* 1990; **18**: 279-307 [DOI: 10.1525/eth.1990.18.3.02a00030]

18 **Matos M**, Pinto-Gouveia J, Gilbert P. The effect of shame and shame memories on paranoid ideation and social anxiety. *Clin Psychol Psychother* 2013; **20**: 334-349 [PMID: 22290772 DOI: 10.1002/cpp.1766]

19 **Carvalho CB**, da Motta C, Pinto-Gouveia J, Peixoto E. Influence of Family and Childhood Memories in the Development and Manifestation of Paranoid Ideation. *Clin Psychol Psychother* 2016; **23**: 397-406 [PMID: 26103941 DOI: 10.1002/cpp.1965]

20 **Kirmayer LJ**, Ryder AG. Culture and psychopathology. *Curr Opin Psychol* 2016; **8**: 143-148 [PMID: 29506790 DOI: 10.1016/j.copsyc.2015.10.020]

21 **Immordino-Yang MH**, Yang XF. Cultural differences in the neural correlates of social-emotional feelings: an interdisciplinary, developmental perspective. *Curr Opin Psychol* 2017; **17**: 34-40 [PMID: 28950970 DOI: 10.1016/j.copsyc.2017.06.008]

22 **Avram M**, Brandl F, Cabello J, Leucht C, Scherr M, Mustafa M, Leucht S, Ziegler S, Sorg C. Reduced striatal dopamine synthesis capacity in patients with schizophrenia during remission of positive symptoms. *Brain* 2019; **142**: 1813-1826 [PMID: 31135051 DOI: 10.1093/brain/awz093]

23 **Howes OD**, McCutcheon R, Owen MJ, Murray RM. The Role of Genes, Stress, and Dopamine in the Development of Schizophrenia. *Biol Psychiatry* 2017; **81**: 9-20 [PMID: 27720198 DOI: 10.1016/j.biopsych.2016.07.014]

24 **McCutcheon R**, Beck K, Jauhar S, Howes OD. Defining the Locus of Dopaminergic Dysfunction in Schizophrenia: A Meta-analysis and Test of the Mesolimbic Hypothesis. *Schizophr Bull* 2018; **44**: 1301-1311 [PMID: 29301039 DOI: 10.1093/schbul/sbx180]

25 **Cheng PWC**, Chang WC, Lo GG, Chan KWS, Lee HME, Hui LMC, Suen YN, Leung YLE, Au Yeung KMP, Chen S, Mak KFH, Sham PC, Santangelo B, Veronese M, Ho CL, Chen YHE, Howes OD. The role of dopamine dysregulation and evidence for the transdiagnostic nature of elevated dopamine synthesis in psychosis: a positron emission tomography (PET) study comparing schizophrenia, delusional disorder, and other psychotic disorders. *Neuropsychopharmacology* 2020; **45**: 1870-1876 [PMID: 32612207 DOI: 10.1038/s41386-020-0740-x]

26 **McCutcheon RA**, Abi-Dargham A, Howes OD. Schizophrenia, Dopamine and the Striatum: From Biology to Symptoms. *Trends Neurosci* 2019; **42**: 205-220 [PMID: 30621912 DOI: 10.1016/j.tins.2018.12.004]

27 **Broyd A**, Balzan RP, Woodward TS, Allen P. Dopamine, cognitive biases and assessment of certainty: A neurocognitive model of delusions. *Clin Psychol Rev* 2017; **54**: 96-106 [PMID: 28448827 DOI: 10.1016/j.cpr.2017.04.006]

28 **Simeone JC**, Ward AJ, Rotella P, Collins J, Windisch R. An evaluation of variation in published estimates of schizophrenia prevalence from 1990─2013: a systematic literature review. *BMC Psychiatry* 2015; **15**: 193 [PMID: 26263900 DOI: 10.1186/s12888-015-0578-7]

29 **Crowe RR**, Roy MA. Delusional disorders. In: Fatemi SH, Clayton PJ. (Eds.), The medical basis of psychiatry. 3rd ed. Totowa (US): Humana Press. 2008: 125-131

30 **González-Rodríguez A**, Esteve M, Álvarez A, Guardia A, Monreal JA, Palao D, Labad J. What we know and still need to know about gender aspects of delusional disorder: A narrative review of recent work. *J Psychiatry Brain Sci* 2019; **4**: e190009 [DOI: 10.20900/jpbs.20190009]

31 **de Portugal E**, González N, Miriam V, Haro JM, Usall J, Cervilla JA. Gender differences in delusional disorder: Evidence from an outpatient sample. *Psychiatry Res* 2010; **177**: 235-239 [PMID: 20334930 DOI: 10.1016/j.psychres.2010.02.017]

32 **González-Rodríguez A**, Molina-Andreu O, Penadés R, Garriga M, Pons A, Catalán R, Bernardo M. Delusional Disorder over the Reproductive Life Span: The Potential Influence of Menopause on the Clinical Course. *Schizophr Res Treatment* 2015; **2015**: 979605 [PMID: 26600949 DOI: 10.1155/2015/979605]

33 **Ravindran AV**, Yatham LN, Munro A. Paraphrenia redefined. *Can J Psychiatry* 1999; **44**: 133-137 [PMID: 10097832 DOI: 10.1177/070674379904400202]

34 **Lemonde AC**, Joober R, Malla A, Iyer SN, Lepage M, Boksa P, Shah JL. Delusional content at initial presentation to a catchment-based early intervention service for psychosis. *Br J Psychiatry* 2020: 1-7 [PMID: 32900414 DOI: 10.1192/bjp.2020.157]

35 **Román Avezuela N**, Esteve Díaz N, Domarco Manrique L, Domínguez Longás A, Miguélez Fernández C, de Portugal E. Gender differences in delusional disorder. *Rev Asoc Esp Neuropsiq* 2015; **35**: 37-51 [DOI: 10.4321/S0211-57352015000100004]

36 **Serretti A**, Lattuada E, Cusin C, Smeraldi E. Factor analysis of delusional disorder symptomatology. *Compr Psychiatry* 1999; **40**: 143-147 [PMID: 10080261 DOI: 10.1016/s0010-440x(99)90118-9]

37 **de Portugal E**, González N, del Amo V, Haro JM, Díaz-Caneja CM, Luna del Castillo Jde D, Cervilla JA. Empirical redefinition of delusional disorder and its phenomenology: the DELIREMP study. *Compr Psychiatry* 2013; **54**: 243-255 [PMID: 23021895 DOI: 10.1016/j.comppsych.2012.08.002]

38 **de Portugal E**, Martínez C, González N, del Amo V, Haro JM, Cervilla JA. Clinical and cognitive correlates of psychiatric comorbidity in delusional disorder outpatients. *Aust N Z J Psychiatry* 2011; **45**: 416-425 [PMID: 21417554 DOI: 10.3109/00048674.2010.551279]

39 **Ellersgaard D**, Mors O, Thorup A, Jørgensen P, Jeppesen P, Nordentoft M. Prospective study of the course of delusional themes in first-episode non-affective psychosis. *Early Interv Psychiatry* 2014; **8**: 340-347 [PMID: 23773323 DOI: 10.1111/eip.12059]

40 **Muñoz-Negro JE**, Ibáñez-Casas I, de Portugal E, Lozano-Gutiérrez V, Martínez-Leal R, Cervilla JA. A Psychopathological Comparison between Delusional Disorder and Schizophrenia. *Can J Psychiatry* 2018; **63**: 12-19 [PMID: 28595494 DOI: 10.1177/0706743717706347]

41 **Hotzy F**, Kerner J, Maatz A, Jaeger M, Schneeberger AR. Cross-Cultural Notions of Risk and Liberty: A Comparison of Involuntary Psychiatric Hospitalization and Outpatient Treatment in New York, United States and Zurich, Switzerland. *Front Psychiatry* 2018; **9**: 267 [PMID: 29973889 DOI: 10.3389/fpsyt.2018.00267]

42 **Baier AL**, Kline AC, Feeny NC. Therapeutic alliance as a mediator of change: A systematic review and evaluation of research. *Clin Psychol Rev* 2020; **82**: 101921 [PMID: 33069096 DOI: 10.1016/j.cpr.2020.101921]

43 **Reeve S**, Sheaves B, Freeman D. The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review. *Clin Psychol Rev* 2015; **42**: 96-115 [PMID: 26407540 DOI: 10.1016/j.cpr.2015.09.001]

44 **Kumar D**. Promoting insight into delusions: Issues and challenges in therapy. *Int J Psychiatry Clin Pract* 2020; **24**: 208-213 [PMID: 31928095 DOI: 10.1080/13651501.2019.1711420]

45 **Daly KD**, Mallinckrodt B. Experienced therapists' approach to psychotherapy for adults with attachment avoidance or attachment anxiety. *J Couns Psychol* 2009; **56**: 549-563 [DOI: 10.1037/a0016695]

46 **Jung E**, Wiesjahn M, Rief W, Lincoln TM. Perceived therapist genuineness predicts therapeutic alliance in cognitive behavioural therapy for psychosis. *Br J Clin Psychol* 2015; **54**: 34-48 [PMID: 25040363 DOI: 10.1111/bjc.12059]

47 **González-Rodríguez A**, Seeman MV. Addressing Delusions in Women and Men with Delusional Disorder: Key Points for Clinical Management. *Int J Environ Res Public Health* 2020; **17**: 4583 [PMID: 32630566 DOI: 10.3390/ijerph17124583]

48 **Kumar D**, Menon M, Moritz S, Woodward TS. Using the back door: Meta-cognitive training for psychosis. *Psychosis* 2014; **7**: 166-178 [DOI: 10.1080/17522439.2014.913073]

49 **Freeman D**, Garety P. Advances in understanding and treating persecutory delusions: a review. *Soc Psychiatry Psychiatr Epidemiol* 2014; **49**: 1179-1189 [PMID: 25005465 DOI: 10.1007/s00127-014-0928-7]

50 **Kellett S**, Totterdell P. Taming the green-eyed monster: temporal responsivity to cognitive behavioural and cognitive analytic therapy for morbid jealousy. *Psychol Psychother* 2013; **86**: 52-69 [PMID: 23386555 DOI: 10.1111/j.2044-8341.2011.02045.x]

51 **Friedman S**. Strategic reframing in a case of "delusional jealousy". *J Strat Syst Therap* 1989; **8**: 1-4 [DOI: 10.1521/jsst.1989.8.2-3.1]

52 **Meichenbaum D**. Core tasks of psychotherapy. What "expert" therapists do. In: The Evolution of Cognitive Behavior Therapy. New York City, Routledge. 2017: 185-194 [DOI: 10.4324/9781315748931-17]

53 **Morrison AP**, Barratt S. What are the components of CBT for psychosis? A Delphi study. *Schizophr Bull* 2010; **36**: 136-142 [PMID: 19880824 DOI: 10.1093/schbul/sbp118]

54 **Leucht S**. Measurements of response, remission, and recovery in schizophrenia and examples for their clinical application. *J Clin Psychiatry* 2014; **75 Suppl 1**: 8-14 [PMID: 24581453 DOI: 10.4088/JCP.13049su1c.02]

55 **González-Rodríguez A**, Estrada F, Monreal JA, Palao D, Labad J. A systematic review of the operational definitions for antipsychotic response in delusional disorder. *Int Clin Psychopharmacol* 2018; **33**: 261-267 [PMID: 29912058 DOI: 10.1097/YIC.0000000000000227]

56 **Lähteenvuo M**, Taipale H, Tanskanen A, Mittendorfer-Rutz E, Tiihonen J. Effectiveness of pharmacotherapies for delusional disorder in a Swedish national cohort of 9076 patients. *Schizophr Res* 2021; **228**: 367-372 [PMID: 33548837 DOI: 10.1016/j.schres.2021.01.015]

57 **Morimoto K**, Miyatake R, Nakamura M, Watanabe T, Hirao T, Suwaki H. Delusional disorder: molecular genetic evidence for dopamine psychosis. *Neuropsychopharmacology* 2002; **26**: 794-801 [PMID: 12007750 DOI: 10.1016/S0893-133X(01)00421-3]

58 **Sajatovic M**, Mbwambo J, Lema I, Carol Blixen C, Aebi ME, Wilson B, Njiro G, Burant CJ, Cassidy KA, Levin JB, Kaaya S. Correlates of poor medication adherence in chronic psychotic disorders. *Br J Psychol Open* 2021; **7**: e23 [DOI: 10.1192/bjo.2020.141]

59 **Thomas RE**, Thomas BC. A Systematic Review of Studies of the STOPP/START 2015 and American Geriatric Society Beers 2015 Criteria in Patients ≥ 65 Years. *Curr Aging Sci* 2019; **12**: 121-154 [PMID: 31096900 DOI: 10.2174/1874609812666190516093742]

60 **Egerton A**, Murphy A, Donocik J, Anton A, Barker GJ, Collier T, Deakin B, Drake R, Eliasson E, Emsley R, Gregory CJ, Griffiths K, Kapur S, Kassoumeri L, Knight L, Lambe EJB, Lawrie SM, Lees J, Lewis S, Lythgoe DJ, Matthews J, McGuire P, McNamee L, Semple S, Shaw AD, Singh KD, Stockton-Powdrell C, Talbot PS, Veronese M, Wagner E, Walters JTR, Williams SR, MacCabe JH, Howes OD. Dopamine and Glutamate in Antipsychotic-Responsive Compared With Antipsychotic-Nonresponsive Psychosis: A Multicenter Positron Emission Tomography and Magnetic Resonance Spectroscopy Study (STRATA). *Schizophr Bull* 2021; **47**: 505-516 [PMID: 32910150 DOI: 10.1093/schbul/sbaa128]

61 **Wolf RCh**, Huber M, Lepping P, Sambataro F, Depping MS, Karner M, Freudenmann RW. Source-based morphometry reveals distinct patterns of aberrant brain volume in delusional infestation. *Prog Neuropsychopharmacol Biol Psychiatry* 2014; **48**: 112-116 [PMID: 24120443 DOI: 10.1016/j.pnpbp.2013.09.019]

62 **Hayashi H**, Akahane T, Suzuki H, Sasaki T, Kawakatsu S, Otani K. Successful treatment by paroxetine of delusional disorder, somatic type, accompanied by severe secondary depression. *Clin Neuropharmacol* 2010; **33**: 48-49 [PMID: 19935408 DOI: 10.1097/WNF.0b013e3181c1cfe4]

63 **O'Connor K**, Stip E, Pélissier MC, Aardema F, Guay S, Gaudette G, Van Haaster I, Robillard S, Grenier S, Careau Y, Doucet P, Leblanc V. Treating delusional disorder: a comparison of cognitive-behavioural therapy and attention placebo control. *Can J Psychiatry* 2007; **52**: 182-190 [PMID: 17479527 DOI: 10.1177/070674370705200310]

64 **Morin L**, Franck N. Rehabilitation Interventions to Promote Recovery from Schizophrenia: A Systematic Review. *Front Psychiatry* 2017; **8**: 100 [PMID: 28659832 DOI: 10.3389/fpsyt.2017.00100]

65 **Vita A**, Barlati S, Ceraso A, Nibbio G, Ariu C, Deste G, Wykes T. Effectiveness, Core Elements, and Moderators of Response of Cognitive Remediation for Schizophrenia: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Psychiatry* 2021; **78**: 848-858 [PMID: 33877289 DOI: 10.1001/jamapsychiatry.2021.0620]

66 **Freeman D**, Bold E, Chadwick E, Taylor KM, Collett N, Diamond R, Černis E, Bird JC, Isham L, Forkert A, Carr L, Causier C, Waite F. Suicidal ideation and behaviour in patients with persecutory delusions: Prevalence, symptom associations, and psychological correlates. *Compr Psychiatry* 2019; **93**: 41-47 [PMID: 31319194 DOI: 10.1016/j.comppsych.2019.07.001]

67 **Sher L**, Kahn RS. Suicide in Schizophrenia: An Educational Overview. *Medicina (Kaunas)* 2019; **55**: 361 [PMID: 31295938 DOI: 10.3390/medicina55070361]

68 **Wong Z**, Öngür D, Cohen B, Ravichandran C, Noam G, Murphy B. Command hallucinations and clinical characteristics of suicidality in patients with psychotic spectrum disorders. *Compr Psychiatry* 2013; **54**: 611-617 [PMID: 23375263 DOI: 10.1016/j.comppsych.2012.12.022]

**Footnotes**

**Conflict-of-interest statement:** Neither author has received fees for serving as a speaker, consultant or advisory board member for any organization related to this review. Neither author has received research funding from any one to conduct this review. Neither author owns stocks or shares in any organization remotely connected with this review. Neither author owns patents related to this review. Neither author reports any conflicts of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** December 18, 2021

**First decision:** March 13, 2022

**Article in press:** April 21, 2022

**Specialty type:** Psychiatry

**Country/Territory of origin:** Canada

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Aedma K, United States; Sahin EK, Turkey; Wang D, China **S-Editor:** Gong ZM **L-Editor:** A **P-Editor:** Gong ZM

**Table 1 Subtypes of delusional disorder in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition[1]**

|  |  |
| --- | --- |
| **Subtypes of delusional content** | |
| Persecutory type | A preoccupation with the belief that one is being persecuted or conspired against |
| Somatic type | A conviction that one’s body is defective or infested or malformed |
| Jealous type | A conviction that one’s lover is unfaithful |
| Grandiose type | A belief that one is somehow superior to others |
| Erotomanic type | A false belief that one has aroused the passionate love of someone important |
| Mixed type | False beliefs that combine the above themes |
| Unspecified type | A vagueness in the expression of one’s beliefs that does not permit sub-classification |

**Table 2 Initial approach to patients with delusional disorder**

|  |  |  |
| --- | --- | --- |
| **Issue** | **Target** | **Recommendation** |
| Safety | For patient, imagined persecutor, and personnel | Safety is the first step |
| Therapeutic alliance | Patient-clinician relationship is crucial (determines adherence to follow-up) | Building trust for working together on common goals |
| Enhancing self-esteem and improving skills | Supporting self-esteem and modeling cognitive and social skills | Improving metacognitive and social skills |
| Targeting emotions and behaviors | Helping patients to identify emotions and prevent acting on delusions | Cognitive-behavioral therapies identify stressors and risk behaviors |

**Table 3 Main interventions for the treatment of delusional disorder and schizophrenia**

|  |  |  |
| --- | --- | --- |
| **Interventions** | **Explanation** | **Remarks** |
| Antipsychotics[57-60] | Antidopaminergic action of these drugs dominates the literature | Genetic studies are inconclusive about the role of dopamine |
| Antidepressants[62] | Antidepressants treat comorbid depression | Reversing depression can sometimes eliminate delusions |
| Cognitive behavioral therapy[63-65] | Addresses cognitive biases and unwanted behavior | Stops adverse behaviors and improves adherence to treatment |



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** bpgoffice@wjgnet.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2022 Baishideng Publishing Group Inc. All rights reserved.**