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The Impact of Psychosis on Sexual Functioning: A Systematic Review

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ABSTRACT

Background: Sexual dysfunction among psychotic patients is highly prevalent. However, most research has focused on antipsychotic side effects on sexual functioning.

Aim: To provide evidence by means of a systematic review of the literature about the impact of psychosis on sexual functioning among unmedicated patients.

Methods: Systematic search of MEDLINE (PubMed), Scopus, and Google Scholar for studies that reported sexual functioning among psychotic patients, who were drug-naïve or drug-free for at least 3 weeks before the study. Studies were published in English language between January 1994 and October 2019. We used the approach recommended by PRISMA, and the selection process was carried out by 2 reviewers.

Outcomes: The outcome measures were sexual function and sexual dysfunctions.

Results: A total of 734 articles were obtained, 658 were obtained after duplicates were removed, 612 were excluded after reading the title and abstract, and 46 were included for a complete review of the articles. 5 papers were finally included. A total of 770 cases were included in the systematic review. The prevalence of sexual dysfunction in psychosis varied from 16.8% to 70% and in ultra-high state was 50%. It is noteworthy that those ultra—high-risk (prodromal) patients who develop psychosis had higher rates of sexual impairment. Therefore, we found higher rates of sexual dysfunction among untreated patients, both psychotic and ultra-high risk patients, than healthy controls.

Clinical Implications: The assessment of sexual behavior should be a part of routine psychiatric examination not only in psychotic but also in ultra—high-risk patients.

Strengths & Limitations: This is the first systematic review about the impact of psychosis on sexual functioning among unmedicated patients. However, scarce and heterogeneous studies were identified.

Conclusions: Impaired sexual functioning is common in the onset of psychosis (or during ultra—high-risk state) and prior to the beginning of treatment. This suggests that psychotic symptoms and sexual dysfunction may have common etiological pathways at the psychosocial and neurobiological levels. **S Vargas-Cáceres, N Cera, P Nobre, et al. The Impact of Psychosis on Sexual Functioning: A Systematic Review. J Sex Med 2020;XX:XXX—XXX.**

Key Words: Psychosis; Sexual Dysfunction; Sexual Motivation; Ultra High Risk; First Episode

INTRODUCTION

Sexual health is an important component of global health and is strongly associated with well-being and life satisfaction.[1,2] Despite the large evidence related to sexual dysfunctions in mood disorders,[3—5] little attention has been given to patients affected by psychotic disorders. Sexual dysfunction is a major cause of poor quality of life and dissatisfaction for the patients and their partners.[6,7] Existing studies indicate that sexual dysfunction among patients with schizophrenia ranges from 30% to 80% in women and from 45% to 80% in men and is more prevalent than what is observed in community samples and in samples of patients with other mental disorders.[8] Dysfunction at different levels of the human sexual response cycle can result as

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an effect of the psychotic disorder, the long-term duration of the disorder, and the comorbid physical disorders.[5] However, most studies focus on sexual functioning among medicated patients[9–12] or the impact of side effects of antipsychotics.[13] According to several studies, antipsychotics are associated with sexual dysfunction[14,15] resulting in a negative attitude to therapy and noncompliance to treatment from the patients.[16] Nonetheless, in other patients, antipsychotic medication may improve sexual functioning compared with untreated patients. In fact, one study indicated that first-generation antipsychotic treatment improves frequency of sexual thoughts and desire for sex, but impairs erection, orgasm, and sexual satisfaction.[17]

It is noteworthy that some studies in the 70s and 80s found an increased sexual drive and hypersexuality during the early stages of psychosis.[18–20] Akhtar and colleagues (1980) described that some sexual disorders may be secondary to the disturbances of thought and perception (ie, delusions with heterosexual or homosexual content, erotic sensations or sexual auditory hallucinations).

In schizophrenic patients, psychological and cultural factors can also contribute to sexual dysfunctions. Studies showed that the experience of unsuccessful sexual events can be interpreted as a failure and a sign of personal incompetence. These negative cognitive schemas once activated elicit negative emotions and automatic thoughts, related to erection concerns and failure anticipation which can impair sexual functioning and also sexual desire.[21,22]

This study aimed to assess the current evidence about the impact of psychosis on sexual functioning in untreated patients through a systematic review of the available literature. To the best of our knowledge, this is the first systematic review about the impact of psychosis on sexual functioning among unmedicated patients.

METHODS

Published studies in English language between January 1994 and October 2019 were selected on databases MEDLINE (PubMed), Scopus, and Google Scholar and by screening the reference lists of articles that reported on the psychotic patients and sexual functioning. We considered only studies published since 1994 in order to keep consistency regarding diagnostic criteria for psychotic disorders (based on DSM-IV or ICD-10, and subsequent editions). We used the approach recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[23]

The computer-based searches follow the PICO approach with combined terms related to psychosis, first-episode of psychosis, schizophrenia, psychotic disorders and study design with those related to sexual activity, sexual function, sexual dysfunction, and sexual disorder. In particular, the population (P) was patients with first-episode of psychosis, schizophrenia, psychotic disorders; the intervention (I) was the assessment with interviews or psychometric tests of sexual functioning; while, the comparison (C) was the comparison between patients and healthy controls; the outcome (O) was sexual functioning assessed as aforementioned.

The articles were included based on the following criteria: patients diagnosed with a psychotic disorder (schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychosis disorder or first-episode of psychosis) according to DSM-IV, DSM-IV-TR, DSM-5, ICD-10 or ICD-11; age range between 15 to 65 years; drug-naïve or drug-free for at least 3 weeks before the study. Also, exclusion criteria included presence of any significant neurological or medical diagnosis (especially intellectual disability and dementia), psychoactive substance use; history of any sexual dysfunction before the symptoms of psychosis; and presence of any other psychiatric diagnosis (except if this diagnosis is produced by psychosis, for example, depressive or anxiety symptoms).

A total of 734 articles were obtained, 658 were obtained after duplicates were removed, 612 were excluded by their title and abstract. The remaining 46 were included for a complete review of the articles. Based on a careful reading of the articles and application of the inclusion and exclusion criteria, 5 papers were finally included in the systematic review. The selection process was carried out by 2 reviewers (N.C and S. V-C.) (Figure 1). To avoid the risk of bias, the 2 authors independently assessed the articles; after that, a discussion has been carried out to reach the consensus between the 2 authors. Researchers came to a consensus over discrepancies through a comprehensive discussion.

Moreover, to avoid the risk of bias and to assess the level of evidence of individual studies, the Newcastle-Ottawa Scale for case-control studies (NOS-ref) was used. We assessed the selected studies on the bases of the dimensions included in the NOS like selection of study groups, comparability of groups, and exposure.

RESULTS

The results from the NOS are reported in the Appendix (Supplementary Table 2).

Study Characteristics

Of the studies included in this review, 60% (n = 3) were conducted in Europe, 20% (n = 1) in Egypt and 20% (n = 1) in India (see Table 1). Four cross-sectional studies and 1 longitudinal study involving a total of 770 cases were included in the systematic review. The longitudinal study was assessed like a cross-sectional one, before initiating antipsychotic drugs.[24]

In our systematic review, 2 studies included patients with first episode of psychosis (n = 65; 8.4%) and one study, patients with ultra high risk for psychosis (n = 31; 4%). It is noteworthy that one study that involved patients with first episode of psychosis was not included, because patients were medicated.[25] Regarding gender, 78.8% were men (n = 749) and 21.2% were women (n = 202) (including cases and healthy controls).

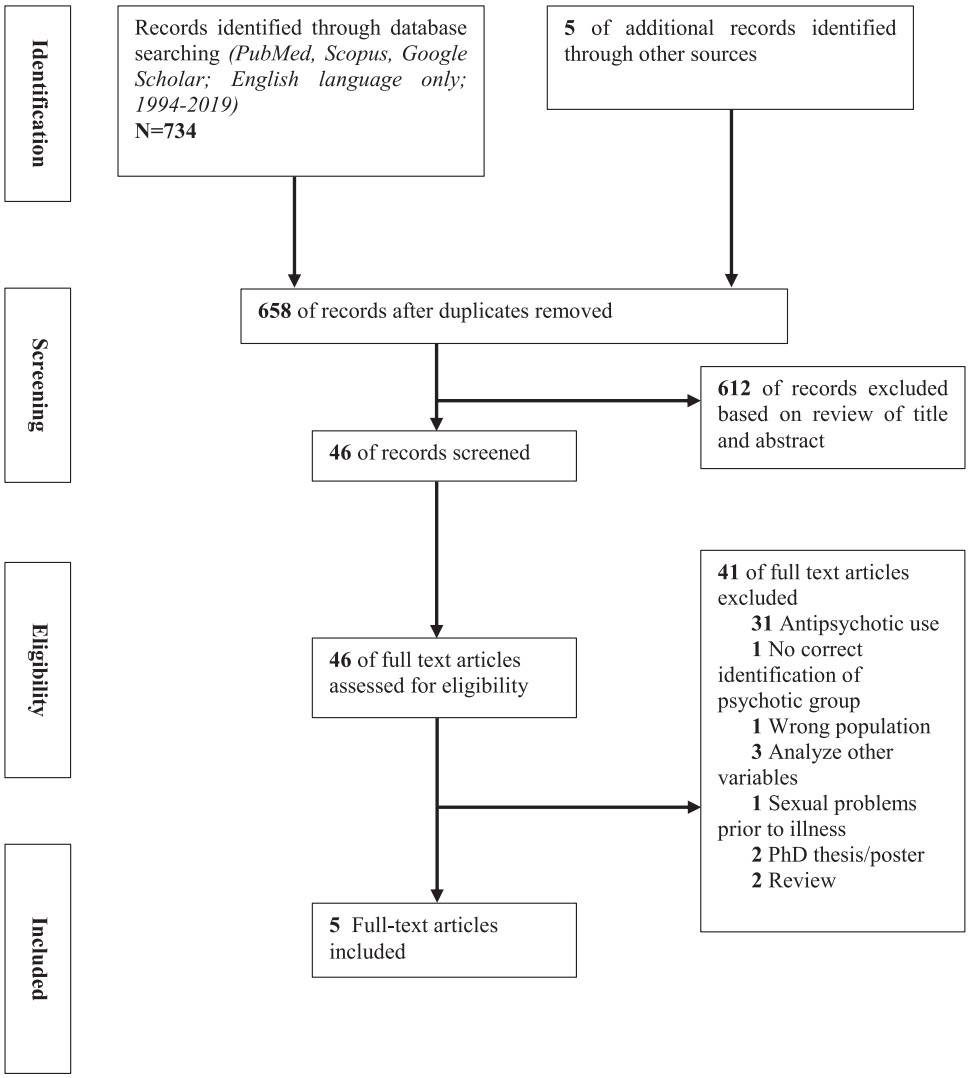

Figure 1. Flow diagram for identifying studies in the systematic review.

Regarding diagnosis, 2 studies used the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) (DSM-IV), 5 used the International Statistical Classification of Diseases and Related Health Problems (ICD-10), and 2 of them used both diagnostic methods. The ultra—high-risk patients were assessed using the Comprehensive Assessment of At-Risk Mental States (CAARMS). For assessing psychopathology, 4 studies used standardized scales: 4 used the Positive and Negative Syndrome Scale (PANSS), for severity of psychotic symptoms, and 2 used additional scales for assessing depressive symptoms (Montgomery-Asberg Depression Rating Scale - MADRS, and Calgary Depression Scale - CDS); another study did not use any additional questionnaire or interview apart from diagnostic assessment. To assess sexual functioning, one study used the Sexual Function Questionnaire (SFQ), one used the International Index of Erectile Function (IIEF), one used the Arizona Sexual Experience Scale (ASEX), one study used the Derogatis Inventory for Sexual Function (DISF-SR) along with an additional sexual anamnesis, and another one assessed this information just through a face-to-face interview. One study used the DSM-IV-TR as further diagnostic assessment for sexual dysfunction.

Regarding hormonal assessment, only one article has measured levels of hormones (testosterone).[26]

Prevalence of Sexual Dysfunction Among Psychotic Patients

Among the studies that investigated overall sexual dysfunction in psychotic patients, the reported prevalence varied from 16.8% to 64%.[24,26,27] Only one study used the distress criterion based on DSM-IV-TR. If one excludes this criterion, the prevalence of sexual dysfunction increased from 17% to 70%.[26]

The prevalence of sexual dysfunction in ultra-high risk (UHR) patients was 50% (in comparison to 21% in the control group), but in the transition group (ie, those who became psychotic) was 83% (in the non-transition group was 42%). It is noteworthy that the UHR transition group had a significantly higher total score on the SFQ (ie, worse sexual functioning) compared with those who

Table 1. Selected characteristics of the 5 articles included in the systematic review

Source	Country	Total number of participants (no. of cases)	Men, no. (%)	Age, y	Design	Diagnosis	Psychopathology assessment	Sexual functioning assessment	Hormonal assessment	Results
Ravichandran et al, 2019[26]	India	100 (100)	100 (100)	18-60	Cross-sectional study	**ICD-10** Acute and transient psychotic disorder (F23) Schizophrenia (F20)	Positive and Negative Syndrome Scale (PANSS).	DSM-IV-TR for male sexual dysfunctions. International Index of Erectile Function scale (IIEF).	Testosterone	**Overall sexual dysfunction (DSM-IV-TR):** 17%. HSDD: 14% (DSM-IV-TR), PE: 5% (DSM-IV-TR), ED 4% (DSM-IV-TR) – 2% (IIEF) and OD 1% (DSM-IV-TR). According IIEF scale, the following results were in mean scores (with SD): Erectile function 14.44 (12.14), Orgasmic function 4.62 (4.87), Sexual desire 5.67 (2.09), Intercourse satisfaction 4.56 (5.18), Overall satisfaction 6 (2.20). **PANSS negative score** had a weak correlation with IIEF subscales of erectile function, orgasmic function, sexual desire, and intercourse satisfaction. **PANSS general psychopathology** correlated with erectile function orgasmic function, sexual desire, and intercourse satisfaction. **PANSS total score** correlated with erectile function orgasmic function, sexual desire, and intercourse satisfaction. **Higher PANSS depression/anxiety factor** was correlated with any type of sexual dysfunction. No association between sexual dysfunction and the severity of illness or testosterone levels.
Sabry et al, 2017[27]	Egypt	100 (50)	100 (100)	<50	Cross-sectional study	**ICD-10** Schizophrenia First-episode of psychosis	Positive and Negative Syndrome Scale (PANSS). Montgomery-Asberg Depression Rating Scale (MADRS).	Arizona Sexual Experience Scale (ASEX)	-	**Overall sexual dysfunction (ASEX)**: 64% in patients and 12% in healthy controls. **ASEX percentages (Sch):** Sexual drive 20%; sexual arousal 44%, penile erection 60%, achieve orgasm 56%, satisfaction with orgasm 56%. **ASEX percentages (control):** Sexual drive 4%; sexual arousal 6%, penile erection 8%, achieve orgasm 10%, satisfaction with orgasm 10%. All were significantly worse in patients than in controls. **Mean ASEX score for Sch:** Mean scores (SD): sexual drive 4.50 (1.82), sexual arousal 3.53 (1.19), penile erection 3.51 (1.52) achieve orgasm 3.46 (1.53) satisfaction with orgasm 3.64 (1.71), total score 19.98 (6.43). **Mean ASEX score for controls**: Sexual drive 2.16 (0.67), sexual arousal 1.02 (0.99), penile erection 1.42 (1.02), achieve orgasm 2.61 (1.01), satisfaction with orgasm 1.14 (1.03), total score 10.78 (2.46). All were significantly worse in patients than in controls. **A long duration of untreated psychosis** was associated with lower scores in penile erection, achieve orgasm, satisfaction with orgasm, and total ASEX scores. **Higher PANSS negative score** was correlated with lower scores in penile erection, achieve orgasm, satisfaction with orgasm, and total ASEX scores. **Higher MADRS score (depressive symptoms)** was associated with lower scores in sexual drive, sexual arousal, achieve orgasm, satisfaction with orgasm, and total ASEX scores. Erectile dysfunction is integrally linked to the psychotic symptoms. **Severity of illness** was positively correlated with sexual dysfunction.

(continued)

Table 1. Continued

Source	Country	Total number of participants (no. of cases)	Men, no. (%)	Age, y	Design	Diagnosis	Psychopathology assessment	Sexual functioning assessment	Hormonal assessment	Results
Dembler-Stamm et al, 2017[28]	Germany	57 (15 First episode, 4 no First episode)	49(85.9)	19-36	Cross-sectional study	**DSM-IV** and **ICD-10** Schizophrenia *First-episode of psychosis*	Positive and Negative Syndrome Scale (PANSS).	Sexual anamnesis The Derogatis Inventory for Sexual Function (DISF-SR)	-	Derogatis sum score (Sch): 61.6 (15.4). Derogatis sum score (controls): 88.0 (26.6). **Mean DISF-SR score (Sch):** sexual cognition and fantasy arousal 17.65 (9.80), arousal 11.98 (5.03), sexual behavior and experience 6.28 (4.62), orgasm 12.07 (4.00) sexual drive, and relationship 12.07 (4.00) **Mean DISF-SR score (controls):** sexual cognition and fantasy 25.08 (10.12), arousal 15.05 (7.45), sexual behavior and experience 13.11 (8.26), orgasm 18.26 (4.46), sexual drive and relationship 16.48 (3.95). Patients reported more problems than controls in all domains, except in arousal domain. Schizophrenic patients had more problems than healthy control group in **sexual anamnesis:** less sexual partners in the last month, first sexual intercourse had been less pleasant, sexuality played a less important role, fewer lifetime number of sexual partners. Significant negative correlations between **PANSS positive score, PANSS negative score, PANSS general psychopathology score, and PANSS total score** with DISF domain (orgasm).
Reis Marques et al, 2012[25]	United Kingdom	124 (31 ultra high risk, 37 first episode—not included)	69 (56)	26.8 ± 6.88 SD	Cross-sectional study	**ICD-10** Pyschotic disorders (F20-F29 and F30-F33) First-episode of psychosis **Comprehensive Assessment of At-Risk Mental States (CAARMS)** Ultra-high risk for psychosis	Positive and Negative Syndrome Scale (PANSS). Calgary Depression Scale (CDS).	Sexual Function Questionnaire (SFQ).	-	**Sexual dysfunction:** UHR: 50% (transition group: 83%; nontransition group: 42%.). Healthy control: 21%. **Mean SFQ score (UHR):** Reduced libido 1.32, arousal problems 1.35, erectile dysfunction 1.36, ejaculatory dysfunction 0.85, vaginal responsiveness 2.27, orgasmic dysfunction 1.93, masturbation 1.76, mean total score 13.16 **Mean SFQ score (controls):** Reduced libido 0.55, arousal problems 0.62, erectile dysfunction 0.57, ejaculatory dysfunction 1.07, vaginal responsiveness 1.60, orgasmic dysfunction 2.02, masturbation 2.73, mean total score 7.5; Differences significant statistically across all domains of sexual function, except for ejaculatory dysfunction, vaginal responsiveness, and masturbation. **Higher total PANSS score** (more severe symptoms) were correlated with **higher SFQ total score** (poor sexual functioning). This was independent of the presence of depressive symptoms, so depression was associated partially to sexual impairment.
Bitter et al, 2005[24]	Austria, Hungary	570 (570)	431 (75.6)	>18	Longitudinal study.	**DSM-IV** or **ICD-10** Schizophrenia	NA	Face-to-face interview	-	Unable to perform sexually: 20.2%, some problems: 16.8%, no problems: 62.9%. There was no significant difference between males and females.

SD = sexual dysfunction; UHR = ultra-high risk; Sch = schizophrenia; HSDD = hypoactive sexual desire disorder; PE = premature ejaculation; ED = erectile disorder; OD = orgasmic disorder; DUP = duration of untreated psychosis; DSM-IV = Diagnostical and Statistical Manual of Mental Disorders, 4th Edition; ICD-10 = International Classification of Diseases, 10th Revision.

did not transition, and the latter group had a higher SFQ total score than the control group.[25] In another study, the Derogatis Inventory for Sexual Function score was significantly lower in psychotic patients than in healthy controls (higher scores indicate better sexual functioning)[28] and in a third study the mean total ASEX score (higher scores mean better sexual functioning) was also significantly lower for psychotic patients than controls.[27]

For specific diagnoses, Ravichandran and colleagues (2019) reported 14% of hypoactive sexual disorder, 5% of premature ejaculation, 4% of male erectile disorder and 1% of orgasmic dysfunction among psychotic patients. It is noteworthy that the authors considered the distress criterion in DSM-IV-TR for reporting these percentages. Another study using the ASEX scale reported sexual drive problems in 20% of the patients, sexual arousal problems in 44%, penile erection difficulties in 60%, problems achieving orgasm in 56%, and dissatisfaction with orgasm in 56%. All percentages (and ASEX sub-scores) were significantly higher in patients than controls.[27] Dembler-Stamm and colleagues (2017) using the DISF-SR scale, found lower scores for schizophrenic patients compared to controls in sexual cognition and fantasy-arousal, sexual behavior and experience, orgasm, sexual drive, and relationship (arousal was the only non-significant difference). The same authors used a clinical interview and found that patients reported more sexual problems than the healthy sample. Indeed, the patients had more difficulties to have sexual partners, their first sexual intercourse had been less pleasant, and sexuality played a less important role.

Regarding the UHR sample, Reis Marques and colleagues (2012) found significantly higher SFQ scores for the patients compared to controls on reduced libido, erectile dysfunction, and orgasmic dysfunction (no significant differences were found for ejaculatory dysfunction, masturbation, and vaginal responsiveness).

Association Between Psychopathology and Sexual Dysfunction

According to the articles included, the severity of the illness assessed by means of total PANSS score was associated with a poor sexual functioning, except in a study from Ravichandran and colleagues (2019).[25,27,28]

Regarding negative psychotic symptoms, most studies described that higher PANSS negative scores were correlated to worse sexual functioning. Ravichandran and colleagues (2019) reported a weak correlation with sexual desire, erectile function, and orgasmic function. Sabry and colleagues (2017) also showed that negative symptoms were associated with lower scores in penile erection and orgasm. However, Dembler-Stamm and colleagues (2017) found an association between negative symptoms and impaired orgasm.

Regarding positive psychotic symptoms, one study reported a significative correlation between positive symptoms and an impaired orgasm.[28]

On the other hand, in the study from Ravichandran and colleagues (2019), higher PANSS depression/anxiety factor was correlated with overall sexual dysfunction. In the study from Sabry and colleagues (2017), higher MADRS score was associated with lower scores in sexual drive, sexual arousal, and orgasm. However, erectile function was not associated with depressive symptoms. According to Reis Marques and colleagues (2017), more severe psychotic symptoms correlated with poor sexual functioning, independent of the presence of depressive symptoms that only partially contributed to sexual impairment.

In a study, long duration of untreated psychosis was associated with lower scores in penile erection, orgasm, and total ASEX score.[27]

Regarding gender, one study indicated that male patients had higher scores on sexual cognition and fantasy arousal domain as well as on orgasm domain than women.[28] However, 2 studies indicated that there was no difference between men and women in the level of sexual performance impairment.[24,25]

Only one study assessed the levels of hormones and has found no association between sexual dysfunction and serum testosterone levels among psychotic patients.[26]

DISCUSSION

A limited number of studies evaluated the impact of psychosis itself on sexual functioning. This systematic review of 5 studies showed a general prevalence of sexual dysfunction in psychotic patients that varied from 16.8% to 70% (when the distress criterion in DSM-IV is excluded) and 50% in ultra—high-risk patients. It is noteworthy that, among ultra—high-risk patients, those who develop psychosis had higher rates of sexual impairment. Overall, we found higher rates of sexual dysfunction among psychotic and ultra—high-risk patients than in healthy population.

The ultra—high-risk state (also known as the "at-risk mental state", and "prodromal") is defined as a prepsychotic phase characterized by attenuated psychotic symptoms, mood alterations, anxiety, and a marked decline in psychosocial functioning.[29,30] It is noteworthy that about 35% of those patients diagnosed with UHR will actually develop a psychotic disorder.[31]

According to our results it is not clear which is the phase of sexual response that is more affected in psychosis. However, the impairment appears to involve all sexual domains from desire to orgasm. Sexual desire dysfunction varies from 14% to 20%, whereas the sexual arousal dysfunction varies from 4% to 60% and orgasm dysfunction from 1% to 56%. The distinct prevalence rates can be justified by the difference in sample selection and sexual assessment criteria. A study among psychotic patients described a low prevalence of sexual dysfunction,[26] even lower than in general population according to previous reports. However, this happened because most did not meet the DSM-IV distress criterion that was used to diagnose sexual dysfunction

among psychotic patients. It is noteworthy that the patients usually underestimated their own sexual dysfunction, and their partners are more concerned about positive psychotic symptoms and poor social functioning.[32] Thus, it can explain the lack of distress and low prevalence obtained in the aforementioned study.

In a study from Dembler-Stamm (2017), sexual arousal was the only domain preserved in patients compared to controls but, according to the authors, the lack of statistical power can explain this result. According to the same authors, these impairments impact on the number of sexual partners, pleasure associated to intercourse, on the probability to have sexual relationships, and on the lesser importance of sexuality in the patients' lives. These factors can explain the reason because schizophrenic patients experience dissatisfaction in their sex life.[33]

Negative and general symptoms (including depression) and their severity are strongly associated with all dimensions of sexual functioning. Therefore, our results are similar with previous reports using medicated patients. [9–12,34,35] However, in one of the included studies,[28] all symptoms, measured by PANSS, affected only the orgasm domain. The authors interpreted this finding as mediated by the hyperprolactinemia that affects especially orgasm.[36] Sabry and colleagues (2017) found that depressive symptoms did not affect erectile function. According to the authors, erectile dysfunction has been influenced directly by psychotic symptoms.

Among positive symptoms, most studies did not report a statistically significant association with sexual functioning. Previous research has reported that hallucinations and delusions with sexual content varies from 14.7% to 26.7% of patients with use of antipsychotics,[37–40] and one study described that 28% had sexual problems related to their positive psychotic symptoms.[39] However, these authors did not describe the relationship between those positive symptoms and specific domains of sexual functioning. According to the literature, positive symptoms could affect differently on domains of sexual functioning.[10,12,41] Depending on its nature, they could influence negatively (ie, auditory hallucinations interfere with desire), or increase sexual drive. For example, in a study on medicated patients with first episode of psychosis, positive symptoms were associated with higher rates of increased libido in both men and women.[12] However, positive symptoms can also provide a rationale for the experience of sexual dysfunction.[39] It is noteworthy that Del Cacho and colleagues (2020) found that disorganized symptoms were associated with worse overall sexual functioning, being desire and arousal domains the most impaired. This study assessed psychosis and sexual functioning with unmedicated patients, but it was not included in our systematic review as authors did not used a formal diagnostic method (DSM-IV or ICD-10).

On the other hand, sexual dysfunction was correlated with the duration of untreated illness. Previous studies have described that long duration of untreated psychosis correlated with more severe negative symptoms[42] and sexual dysfunction.[43] However, a recent study did not find any association with sexual dysfunction.[41]

In the present review, depressive symptoms in psychotic disorders were negatively associated with most domains in sexual functioning, but its association contributed partially to sexual impairment in a study. Previous reports with medicated patients found a similar association.[9,10,35]

Regarding gender, the included studies were controversial. Previous studies with medicated patients reported a gender-specific correlation between sexual dysfunctions (ie, alteration of vaginal lubrication and orgasm) and psychopathological symptoms, which stronger affected women.[9] Similarly, in a study from Del Cacho and colleagues (2020), psychotic women showed worse sexual functioning than men. Conversely, 2 studies found similar association in both male and female patients.[10,12]

With regard to endocrine factors, only one study reported hormonal assessment without finding an association between sexual dysfunction and serum testosterone levels among patients.[26] Del Cacho et al (2020) found similar results in the comparison between patients and healthy controls. However, many individuals with decreased sexual desire have concomitant endocrine dysregulation, including decreased plasma testosterone and hyperprolactinemia.[44] In fact, testosterone plays an important role in different phases of the sexual response.[45–47] On the other hand, hyperprolactinemia is associated with low sexual desire in both genders[48] and erectile, ejaculatory and, in particular, orgasm problems in men.[36,49,50] Antipsychotic-naïve patients with schizophrenia and people at high risk for psychosis have significantly increased prolactin concentrations compared to healthy subjects[36,41,51] probably as part of the stress response.[52] A study that assessed sexual functioning and prolactin in first-episode psychosis[41] did not find any correlation between hyperprolactinemia and sexual impairment. On the other hand, Malik and colleagues (2011) reported that higher plasma prolactin rates are related to both erectile and ejaculatory dysfunctions in medicated psychotic patients. Thus, more evidence is needed to test the role of prolactin on sexual dysfunction of drug-naïve psychotic patients.

Among the etiological pathways that can explain sexual dysfunctions in unmedicated psychotic patients, we also can consider neural and psychosocial factors.

Recent studies about the neurobiological correlates of human sexual behavior highlighted the role played by several regions involved in the dopaminergic pathway, like the ventral striatum, playing an important role in the motivation and sexual drive.[53,54]

It is widely recognized as the critical role of brain dopamine in the pathophysiology of schizophrenia. Striatal dopaminergic dysregulation plays a crucial role in positive symptoms[55,56] but it is also related to negative and cognitive symptoms interfering with the neural processing of reward-predicting cues[57] and

reducing motivational drive.[58–60] This striatal dopaminergic dysfunction is already present at ultra–high-risk state.[61,62] However, none of the selected studies directly investigated the dopaminergic dysregulation, but future studies could assess the relationship between sexual desire and arousal dysfunction in psychosis and dopaminergic dysregulation.

Finally, stigma, low self-esteem, difficulty in communication skills, beliefs about rejection and criticism from others, or negative cognitive schemas because of the experience of unsuccessful past sexual events are psychosocial factors that should be taken account in UHR and psychotic patients.[63]

Our study has to be interpreted in the context of some limitations. First, studies were scarce and heterogeneous in diagnostic methods. Second, most studies were cross-sectional, except one that was longitudinal, but assessed sexual functioning only at the beginning. Third, a substantial amount of the heterogeneity in the assessment of sexual functioning among the studies did not allow to compare specific domains (eg, desire, arousal, orgasm). Fourth, most studies had small sample sizes. Fifth, all except one had no information on the levels of hormones such as sex hormones and prolactin, and their impact on sexual functioning. Sixth, most studies did not assess other potential psychosocial factors that may had exerted a role in the association between psychotic patients and sexual functioning (eg, beliefs focused on sexual failure and low self-esteem). Finally, studies had no information about sexual functioning before the onset of disease.

CONCLUSIONS

Impaired sexual functioning is common in the onset of psychosis or during ultra-high risk state, and before the beginning of treatment. This suggests that sexual dysfunction is intrinsic to the development of illness. The link between psychotic symptoms and sexual functioning suggests that probably they share common etiological pathways both at the psychosocial and neurobiological dimensions.

According to our results, negative and general symptoms (including depression) had a more significant association with sexual dysfunction than positive symptoms. This sexual impairment appeared to involve all sexual dimensions, from desire to orgasm. More evidence is required to establish that hormones are implicated in sexual dysfunction in unmedicated patients. The role of gender was controversial and further research is also needed.

Regarding the high prevalence of sexual dysfunction among these patients, we recommend a thorough sexual assessment. It should be a part of routine psychiatric examination not only in psychosis but also in ultra–high-risk patients. Probably, sexual dysfunction among UHR patients could be a "prodromal symptom" to identify those who are at more risk to develop psychosis. This evaluation should assess how cognitive and psychopathological symptoms affect sexual functioning. Clinicians should consider that a percentage of patients could not be stressed by sexual dysfunction, and this should be taken into account. Therefore, it is relevant to assess the importance of sexuality for each patient. Such a procedure may play an important role in improving not only adherence to psychiatric treatment and follow-up but quality of life and sexual satisfaction.

From a methodological point of view, we strongly suggest a better ratio between women and men. On the other hand, future studies should have a longitudinal or prospective design. This assessment will contribute to distinguish between the disease process and dysfunction induced by prolactin-increasing properties of the antipsychotic medications. Moreover, an assessment from a prepsychotic state to psychosis will allow to know how sexual functioning is affected by different phases of development of illness. We advise to measure sexual functioning before and during the onset of disease with standardized questionnaires or clinical assessment for each sexual dysfunction domain. The inclusion of qualitative studies, describing the content of delusions or hallucinations with sexual characteristics and its relationship with sexual functioning domains is recommendable. Finally, we think that researching the underlying psychosocial and neurobiological processes of sexual dysfunction in patients with psychosis and ultra–high-risk state could provide new insights to understand sexual functioning.

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STATEMENT OF AUTHORSHIP

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Conceptualization, Methodology, Investigation, Resources, Writing - Review & Editing, Funding Acquisition; Josep Antoni Ramos-Quiroga, Conceptualization, Methodology, Investigation, Resources, Writing - Review & Editing, Funding Acquisition.

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SUPPLEMENTARY DATA

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