

The accuracy of the Arizona Sexual Experience Scale (ASEX) to identify sexual dysfunction in patients of the schizophrenia spectrum

A acurácia da Escala de Experiência Sexual do Arizona (ASEX) para identificar disfunção sexual em pacientes do espectro da esquizofrenia

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Abstract

Background: Sexual dysfunction is frequent in patients with schizophrenia, it is reported as one of the most distressing antipsychotic's adverse effects and it is directly related to treatment compliance. **Objectives:** a) to evaluate the accuracy of the Arizona Sexual Experience Scale (ASEX) to identify sexual dysfunction; b) to assess the frequency of sexual dysfunction in a sample of outpatients with schizophrenia and schizoaffective disorder under antipsychotic therapy; and c) to investigate the effect of different antipsychotics on sexual function. **Method:** Outpatients with schizophrenia or schizoaffective disorder were asked to fulfill both the ASEX and the Dickson Glazer Scale for the Assessment of Sexual Functioning Inventory (DGSFi) at a single interview. **Results:** 137 patients were interviewed. The sensitivity and specificity of the ASEX in relation to DGSFi were: 80.8%, (95% CI = 70.0%-88.5%) and 88.1% (95% CI = 76.5%-94.7%), and the misclassification rate was 9.5%. The ROC curve comparing the ASEX and the DGSFi scores revealed a value of 0.93 (CI = 0.879-0.970), with the optimum cut-off point of ASEX being 14/15. Sexual dysfunction measured was higher in females (79.2%) than in males (33.3%) ($\chi^2 = 27.41$, d.f. = 1, $p < 0.001$). **Discussion:** Patients under antipsychotic treatment showed a high level of sexual complaints, and the ASEX proved to be an accurate instrument to identify sexual dysfunction in an outpatient sample of patients with schizophrenia spectrum. Females showed a higher frequency of sexual dysfunctions and sexual drive and ability to reach orgasm were the most affected areas. The use of antipsychotics, especially the combinations, was more likely to impair sexual functioning.

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Keywords: Schizophrenia, sexual dysfunction, antipsychotics, ASEX.

Resumo

Contexto: A disfunção sexual é frequente entre pacientes com esquizofrenia, sendo relatada como um dos mais incômodos efeitos adversos dos antipsicóticos e está diretamente relacionada com a adesão ao tratamento. **Objetivos:** a) avaliar a acurácia da Escala de Experiência Sexual do Arizona (ASEX) para identificar disfunção sexual; b) avaliar a frequência da disfunção sexual em uma amostra de pacientes do espectro da esquizofrenia em tratamento com antipsicóticos; e c) investigar o efeito dos diferentes antipsicóticos na função sexual. **Método:** Foram entrevistados

pacientes ambulatoriais com esquizofrenia ou transtorno esquizoafetivo por meio dos questionários ASEX e Escala Dickson-Glazer (DGSFi) para avaliação do funcionamento sexual, em uma única entrevista. **Resultados:** 137 pacientes foram entrevistados. A sensibilidade e a especificidade da ASEX em relação à DGSFi foram: 80,8% (95% IC = 70,0%-88,5%) e 88,1% (95% IC = 76,5%-94,7%), e a taxa de classificação incorreta foi 9,5%. A curva ROC comparando a pontuação da ASEX e a DGSFi revelou valor de 0,93 (IC = 0,879-0,970) com o ponto de corte da ASEX encontrado sendo 14/15. A disfunção sexual foi mais alta entre as mulheres (79,2%) do que nos homens (33,3%) ($\chi^2 = 27,41$, $gl = 1$, $p < 0,001$). **Conclusão:** Os pacientes em tratamento com antipsicóticos mostraram alta frequência de queixas sexuais e a ASEX provou ser um instrumento eficaz para identificar disfunção sexual em amostra de pacientes ambulatoriais do espectro da esquizofrenia. As mulheres mostraram frequência mais alta de disfunção, e o desejo sexual e a habilidade para alcançar orgasmo foram as áreas mais afetadas. O uso de antipsicóticos, principalmente o uso de combinações, foi associado com a piora do funcionamento sexual.

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Palavras-chaves: Esquizofrenia, disfunção sexual, antipsicóticos, ASEX.

Introduction

Long term treatment is indicated for all patients with schizophrenia¹. Antipsychotic drugs can be of great benefit for a wide range of psychotic disorders, although treatment can be associated with potential and unpleasant adverse effects². Antipsychotic drugs may restore sexual desire lost for patients with schizophrenia, but they can also impair the patient's sexual performance^{3,5}. Antipsychotics can cause sexual dysfunction through multiple mechanisms, including sedation, hyperprolactinaemia (which can cause sexual dysfunction directly and indirectly by causing secondary hypogonadism) and antagonism of α -adrenergic, dopaminergic, histaminic and muscarinic receptors². Moreover, there are many other factors that may cause sexual problems for patients with schizophrenia, including concomitant medications, the effect of the disease itself, comorbidity with other psychiatric disorders and various endocrine, vascular or genitourinary diseases⁶. Negative symptoms of the disorder, such as anhedonia, avolition and blunted affect related to hypodopaminergic activity in the frontal cortex, severely harm the ability to enjoy sexual life. These patients face difficulties in establishing relationships due to recurrent psychotic episodes, obesity and low self-esteem⁷.

It is noteworthy that a recent study conducted by Plevin et al.⁸ reported that 73% of men presented complaints in at least one area of antipsychotic-induced sexual dysfunction: a) erectile, ejaculatory, and orgasmic dysfunction⁹⁻¹⁶ b) low sexual desire^{11,13-16} and c) priapism¹². Although fewer studies have been conducted with females, there is evidence of sexual dysfunctions in the following areas: a) lack of orgasm^{11,13,17,18} b) low lubrication^{13,19} c) loss of libido^{14,19} and d) amenorrhea¹¹. Sexual dysfunctions induced by antipsychotic treatment can be responsible for non-adherence to treatment²⁰ and non compliance is one of the main obstacles to an adequate control of the symptoms present in patients

with schizophrenia². Moreover, sexual dysfunction is rated as one of the most distressing adverse effects of antipsychotic treatment^{22,23} and experienced by patients as significantly more distressing than sedation, or extrapyramidal side effects²².

At present, there are three scales available to assess sexual dysfunctions in patients under antipsychotic treatment: a) the Dickson and Glazer Scale for the Assessment of Sexual Functioning Inventory (DGSFi)²⁴; b) the Arizona Sexual Experience Scale (ASEX)²⁵; c) the Psychotropic-Related Sexual Dysfunction (PRSexDQ-SALSEX)²⁶. Unlike the more traditional and lengthy scales for assessing sexual dysfunctions, the ASEX can be completed in approximately 5 minutes²⁷ and it was designed to be self- or clinician-administered. In addition, the ASEX questionnaire can be used for heterosexual and homosexual populations, as well as for those without sexual partners²⁸.

Antipsychotic-induced sexual dysfunctions are poorly recognized, and not properly investigated by most clinicians²⁹. Thus, it is very important to have accurate tools to aid clinicians in the diagnosis of antipsychotic-induced sexual dysfunctions²⁸. The main aims of this paper are threefold: a) to evaluate the accuracy of the ASEX to identify sexual dysfunction; b) to assess the frequency of sexual dysfunction in a sample of outpatients with schizophrenia and schizoaffective disorder under antipsychotic therapy; and c) to investigate the effect of different antipsychotics on sexual function.

Methods

A cross-sectional study of sexual function was conducted with 1-year consecutive outpatients from the Schizophrenia Program of the Universidade Federal de São Paulo (Proesq), from February 2007 to January 2008. The study was submitted and approved by the Ethics Committee of the Universidade Federal de São Paulo, and participants signed a written informed consent to

participate. Eligible subjects recruited were stabilized outpatients who met DSM-IV criteria for schizophrenia and schizoaffective disorder under antipsychotic therapy for at least four weeks. The patients were currently receiving a fixed dose of a first- or second-generation antipsychotic (risperidone was analyzed separately since it is an antipsychotic that frequently causes hyperprolactinaemia), or a combination of first- and second-generation antipsychotics, or a combination of antipsychotics and antidepressants. Patients consecutively attending the outpatient clinic were asked to fulfill a questionnaire comprising information on social and demographic characteristics, clinical symptoms, pharmacologic treatment, substance use disorders, sexual function, presence of partner, and time of disease onset, followed by the application of the ASEX and the DGSFi.

Instruments

The DGSFi was developed by Ruth Dickson and William Glazer in the University of Calgary, Canada, to assess sexual dysfunctions in patients suffering from schizophrenia spectrum disorders. It is a computerized assessment, categorical and qualitative, of sexual functioning and was developed to be easy for the researcher to obtain detailed information reducing embarrassment and discomfort for patients. The DGSFi is a computerized self-report questionnaire of sexual functioning with parallel versions developed for males (32 questions) and females (41 questions). It is a multiple choice questionnaire aiming to assess sexual activity frequency, desire, arousal, and orgasm for both solitary and partner sexual activities and perceptions of medication side effects for the prior 2 weeks²⁴. A Brazilian version of the DGSFi was adapted and used by Costa et al.³⁰ to compare the frequency of sexual dysfunction between first-generation antipsychotic treatment and olanzapine.

The ASEX was developed by McGahuey et al. in the University of Arizona in response to the need for evaluating psychotropic drug-induced sexual dysfunction. Initially, the scale was tested to assess sexual dysfunction among selective serotonin reuptake inhibitor (SSRI)-treated subjects²⁵ and end-stage renal disease³¹. Byerly et al. tested the psychometric properties of ASEX in patients with schizophrenia and schizoaffective disorder and demonstrated that ASEX represents an easy-to-administer tool for assessing sexual dysfunction in this population²⁸. The ASEX is a brief 5-item questionnaire designed to measure sexual functioning in the following domains: sexual drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm, and satisfaction with orgasm over the past week²⁵. Items are rated on a 6-point scale ranging from 1 (hyperfunction) through to 6 (hypofunction), providing a total score range between 5 and 30. A total score > 18, or a score ≥ 5 (very difficult) on any single item or

any three items with individual scores ≥ 4 is indicative of clinically significant sexual dysfunction.

Results

The sociodemographic and clinical characteristics of the sample can be seen in table 1. The sample was comprised of 137 patients, with an excess of males (61.3%). The mean age of the sample was 37 ± 10.3 years. Most patients were Caucasians (62.0%), with a mean of 11.6 ± 4.1 years of schooling. Most patients were unemployed (78.1%). Most patients were single (82.6% men and 78.4% women), and only few patients (2.9%) were married (3.5% of men and 2% of women), or had a stable partner (9.3% of men and 3.9% of women). The mean duration of illness was 14.4 ± 9 years, with no difference between sexes. Patients on second-generation antipsychotics (without risperidone) corresponded to 46.7% ($n = 64$) of the sample and patients on first-generation antipsychotics corresponded to 16.1% ($n = 22$). Risperidone was used by 14 patients (10.2%). Combination of antipsychotics was taken by 13 patients (9.5%) and combined antipsychotics and antidepressants were prescribed to 24 patients (17.5%).

All the patients ($n = 137$) filled both questionnaires (ASEX and DGSFi). The internal consistency of the ASEX was estimated by means of the Cronbach's α coefficient ($\alpha = 0.81$), and mean Pearson's correlation for the five ASEX items was 0.47. Table 2 displays the distribution of the ASEX scores against the DGSFi scores. As it can be seen in Table II, sensitivity was 80.8% (95% CI = 70-88.5), specificity was 88.1% (95% CI = 76.5-94.7), predictive positive value (PPV) was 90% (95% CI = 79.9-95.5), and negative predictive value (NPV) was 77.6% (95% CI = 65.5-86.5). The misclassification rate was 9.5%. As it can be seen in figure 1 the comparison between the ASEX and the DGSFi scores resulted in an area under the curve value of 0.93 ± 0.021 (95% CI = 0.88-0.97, $p = 0.0001$). The ASEX cut-off point for sexual dysfunction was found to be 14/15.

Table 3 displays the distribution of penile erection or vaginal lubrication dysfunction according to type of treatment. The highest percentage of dysfunction occurred for patients under the combination of antipsychotics (61.5%), followed by combined antipsychotics and antidepressants (50%). Patients under second-generation antipsychotics presented a higher probability of dysfunction (28.1%) than those under first-generation antipsychotics (13.6%), the difference being statistically significant (Fisher's exact test, $p = 0.00108$).

For the ASEX items sexual drive, arousal, and satisfaction, there were no statistical differences across treatments.

Table 4 displays the distribution of sexual dysfunction between genders across the pharmacological interventions. Sexual dysfunction measured by ASEX was higher in females (79.2%) than in males (33.3%), and the dif-

Table 1. The sociodemographic and clinical characteristics of the schizophrenia spectrum outpatients.

	Male	Female	Total	p Value
Gender (n e %)	84 (61.3%)	53 (38.7%)	137	< 0.001
Age, years (mean, SD)	36.7 (SD = 9.6)	37.5 (SD = 11.4)	37.0 (SD = 10.3)	0.663 ^t
Marital Status (n e %)				
Married	3 (3.5%)	1 (2.0%)	4 (2.9%)	0.144 ^f
Stable Partner	8 (9.3%)	2 (3.9%)	10 (7.3%)	
Single	69 (82.6%)	42 (78.4%)	111 (81.0%)	
Widow	–	2 (3.9%)	2 (1.5%)	
Divorced	4 (4.7%)	6 (11.8%)	10 (7.3%)	
Race/Ethnicity (n e %)				
Caucasians	55 (65.5%)	30 (56.6%)	85 (62.0%)	0.673 ^q
Asians	10 (11.9%)	11 (20.8%)	21 (15.3%)	
Africans	2 (2.4%)	2 (3.8%)	4 (2.9%)	
Mestizos	9 (10.7%)	5 (9.4%)	14 (10.2%)	
Others	8 (9.5%)	5 (9.4%)	13 (9.5%)	
Mean years of schooling	11.8 (SD = 4.1)	11.4 (SD = 4.0)	11.6 (SD = 4.1)	0.632 ^t
Employment Status				
Unemployed	65 (77.4%)	43 (81.1%)	108 (78.8%)	0.601 [†] q
Employed or Studying	19 (22.6%)	10 (18.9%)	29 (21.2%)	
Illness Duration (years, mean, SD)	14.4 (SD = 9.1)	14.0 (SD = 8.8)	14.4 (SD = 9.0)	0.779 ^t
Medications				
First Generation	11 (13.1%)	11 (20.8%)	22 (16.1%)	0.062 [‡] q
Second Generation	46 (54.8%)	18 (34.0%)	64 (46.7%)	
First + Second Generation	5 (6.0%)	8 (15.1%)	13 (9.5%)	
Risperidone	10 (11.9%)	4 (7.5%)	14 (10.2%)	
Antipsychotics + antidepressants	12 (14.3%)	12 (22.6%)	24 (17.5%)	
Number of admissions	3.6 (SD = 11.3)	2.2 (SD = 2.3)	2.4 (SD = 3.5)	0.468 [§] u
Sexual Dysfunction	28 (33.3%)	42 (79.2%)		p < 0.001 [†] q

^t Student's t test; [†] Fisher's exact test; [‡] Chi-square test; [§] Mann-Whitney test.

Table 2. The validity coefficients comparing the ASEX scores against the DGSFi scores.

	DGSFi Dysfunction	DGSFi No dysfunction	Total	
ASEX Dysfunction	63	7	70	PPV = 90.0 (CI = 79.9-95.5)
ASEX No dysfunction	15	52	67	NPV = 77.6 (CI = 65.5-86.5)
Total	78	59	n = 137	
	Sensitivity = 80.8 (CI = 70-88.5) Specificity = 88.1 (CI = 76.5-94.7)			
ASEX score	20.56 ± 4.85	11.16 ± 3.72	15.96 ± 6.39	p = 0.001 (Mann Whitney test)

Table 3. The distribution of sexual dysfunction given by the ASEX questionnaire according to the pharmacological treatment.

Medication	Penis erec/Vaginal lub (male and female)	
	No dysfunction N %	With dysfunction N %
First-generation Antipsychotics	19 (86.4%)	3 (13.6%)
Second-generation Antipsychotics	46 (71.9%)	18 (28.1%)
Risperidone	11 (78.6%)	3 (21.4%)
Combination of antipsychotics	5 (38.5%)	8 (61.5%)
Antipsychotics and Antidepressants	12 (50%)	12 (50%)

Fisher's exact test = p = 0.0108

ference was statistically significant (chi-square = 27.41, d.f. = 1, $p < 0,001$). The mean ASEX scores for females ($19.53 \pm 5,69$) was higher than those found for males (13.71 ± 5.78), and this difference was statistically significant ($t = 5.77$, d.f. = 1, $p < 0,001$). Females were more likely to have higher difficulty in sexual drive than males when using medications, the difference

being statistically significant (Fisher's exact test, $p = 0.0131$). Moreover, females had higher probability of dysfunction in reaching orgasm than males when under pharmacological interventions, the difference being statistically significant (Fisher's exact test, $p = 0.0225$). The distribution of sexual dysfunction by gender in the ASEX scores can be seen in table 5. Sexual functions as sexual drive ($\chi^2 = 19.38$, d.f. = 1, $p < 0.001$), sexual arousal ($\chi^2 = 14.29$, d.f. = 1, $p < 0.001$), orgasm ($\chi^2 = 26.17$, d.f. = 1, $p < 0.001$) and satisfaction with orgasm ($\chi^2 = 12.26$, d.f. = 1, $p < 0.001$) occurred in higher frequency in females than in males, and these differences were all statistically significant.

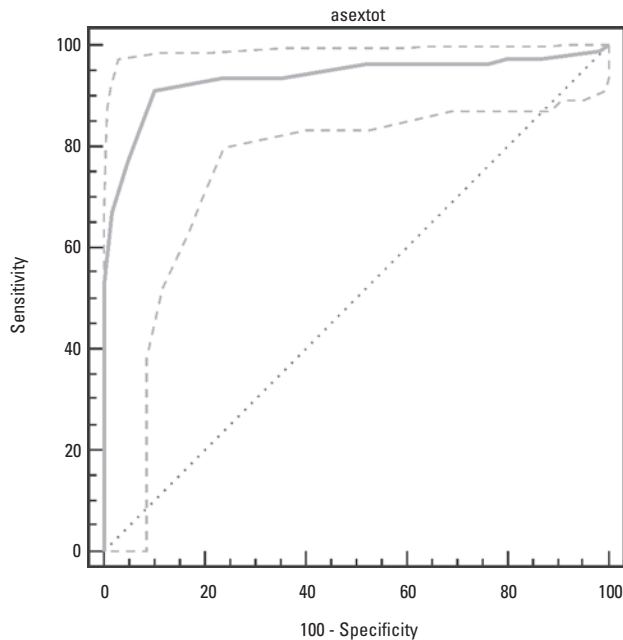


Figure 1. The ROC curve and 95% confidence interval, comparing the ASEX and the DGSFi scores.

Table 5. The ASEX gender distribution of sexual dysfunction in an outpatient sample of patients of the schizophrenia spectrum.

	Male		Female		Total		p-value
	n	%	n	%	n	%	
Sexual drive	22	26.2	34	64.2	56	40.9	< 0.001
Sexual arousal	22	26.2	31	58.5	53	38.7	< 0.001
Penis erection/ Vaginal lubrification	20	23.8	24	45.3	44	32.1	0.009
Orgasm	20	23.8	36	67.9	56	40.9	< 0.001
Satisfaction with orgasm	16	19.0	25	47.2	41	29.9	< 0.001

Table 4. The ASEX gender sexual distribution across pharmacological interventions in an outpatient sample of patients of the schizophrenia spectrum.

	Second generation	First generation	Risper.	First + second generation	Antipsyc + Antidep	p-value*
Female	n = 18	n = 11	n = 4	n = 8	n = 12	
Male	n = 46	n = 11	n = 10	n = 5	n = 12	
Sexual Drive						
Female	12 (66.7%)	6 (54.6%)	–	8 (100.0%)	8 (66.7%)	0.0131
Male	13 (28.3%)	2 (18.2%)	3 (30.0%)	1 (20.0%)	3 (25.0%)	0.9821
Arousal						
Female	11 (61.1%)	5 (45.5%)	1 (25.0%)	6 (75.0%)	8 (66.7%)	0.4585
Male	13 (28.3%)	1 (9.1%)	4 (40.0%)	1 (20.0%)	3 (25.0%)	0.6044
Penis errec/Vaginal lubr						
Female	6 (33.3%)	3 (27.3%)	1 (25.0%)	5 (62.5%)	9 (75.0%)	0.0802
Male	12 (26.1%)	–	2 (20.0%)	3 (60.0%)	3 (25.0%)	0.1041
Orgasm						
Female	12 (66.7%)	5 (45.5%)	1 (25.0%)	8 (100.0%)	10 (83.3%)	0.0225
Male	13 (28.3%)	2 (18.2%)	3 (30.0%)	1 (20.0%)	1 (8.3%)	0.6664
Satisfaction						
Female	10 (55.6%)	3 (27.3%)	1 (25.0%)	5 (62.5%)	6 (50.0%)	0.4573
Male	10 (21.7%)	–	4 (40.0%)	–	2 (16.7%)	0.1578

* Fisher's exact test.

Discussion

The ASEX questionnaire proved to be an accurate instrument to identify sexual dysfunction when compared to the validity of the DGSFi questionnaire. Sensitivity and specificity were fairly high at a c.o. p. = 14/15. It is a friendly self-administered questionnaire, which takes a few minutes to be completed and is appropriate for individuals with or without stable sexual partners and for heterosexual or homosexual patients^{27,28}. It was decided to use the DGSFi questionnaire as a gold standard because it was the only one adapted for a Brazilian social and cultural context. The DGSFi was applied by Costa et al.³⁰ to compare the frequency of sexual dysfunction among patients with schizophrenia between first-generation antipsychotic treatment and olanzapine. DGDFi is a detailed and length self-report scale with 32 questions to assess sexual functioning for males and 41 questions for females in respect to sexual activity frequency, desire, arousal and orgasm and perceptions of medications side effects in the prior 2 weeks. Unlike the more traditional and lengthy scales for assessing sexual dysfunctions, the ASEX can be completed in approximately 5 minutes²⁷, it is a brief 5-item questionnaire designed to measure sexual functioning in the following domains: sexual drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm, and satisfaction with orgasm over the past week²⁵.

The frequency of sexual dysfunctions was very high, a finding consistent with previous studies conducted in different countries^{6,11,15,32-35}. Females had a much higher rate (79.2%) than males (33.3%). Indeed, females reported high frequencies of sexual dysfunctions in all stages of sexual activities (sexual drive, arousal, vaginal lubrication, ability to reach orgasm and satisfaction with orgasm). This difference between genders can be attributed to biopsychosocial factors, in special: sexual hormones (estrogens × androgens), sexual education (repressing × permissive), environment (controlling × stimulant)³⁶.

Patients under second-generation antipsychotics had a higher probability of dysfunction (28.1%) than those under first-generation antipsychotics (13.6%). Antipsychotic medications were associated to disturbance on penile erection and vaginal lubrication reported in ASEX questionnaire and had scores ranging progressively for first-generation antipsychotics (13.6%), second-generation antipsychotics without risperidone (28.1%), risperidone (21.4%), combination of antipsychotics (61.5%), or combination of antipsychotics and antidepressants (50%).

Although new second-generation antipsychotics were expected to be associated with a lower incidence of sexual dysfunction as compared with first-generation antipsychotic medications³⁷⁻⁴⁴, other studies have not confirmed these findings^{6,15,22,30}. Increased prolactin levels are believed to play a major role in sexually

induced side effects, but the underlying mechanism of antipsychotic agent-induced sexual dysfunction remains poorly understood⁴⁵. Contrary to the fact that the causes for sexual dysfunction of antipsychotics were exclusively secondary to hyperprolactinemia, is that clozapine produced little or no change on serum prolactin concentration⁴⁶, but high rates of sexual side effects in a prospective drug monitoring program⁴⁷. Because of the scarcity of comparative studies, conflicting data and methodological issues, the interpretation of the findings of antipsychotics leading to sexual dysfunctions are inconclusive².

In our study, the pharmacological interventions were different between genders: women under long-term treatment with antipsychotics, especially with combinations of antipsychotics or antipsychotics and antidepressants, had significantly more sexual dysfunction in the items related to sexual drive ($p = 0.0131$) and orgasm ($p = 0.0225$); men had no significant difference between the items when analyzed separately. This difference may be explained because women are clearly more sensitive than men to the effects of antipsychotics on prolactin⁴⁸⁻⁵⁰. In a 6-week study, 63% of haloperidol-treated men, compared with 98% of haloperidol-treated women had a prolactin level above the upper limit of normal⁴⁸. There are few systematic data available regarding the frequency of impaired sexual interest or function with antipsychotic treatment, and almost all studies are cross-sectional⁵¹. Although less research on this subject has been conducted in women than in men with schizophrenia, there is evidence that sexual and hormonal dysfunction is also common in antipsychotic-treated women. In addition, 33% of women complained of change in quality of orgasm in a cross-sectional study⁵². One study comparing sexual side effects in patients treated with haloperidol and clozapine found similar proportions treated with both antipsychotics and reported decreased sexual desire in 28-33% of women⁴⁷. Another study examining sexual function in women treated with typical antipsychotics found a similar proportion (22%), reporting decreased ability to achieve orgasm with antipsychotic treatment¹⁷. There is a need of sexual dysfunction studies including women. Many clinical studies have tended to enlist few women or have excluded them altogether⁵³. Women may underreport the frequency of sexual side effects because they are embarrassed to discuss this topic. There is a naturalistic study of galactorrhea incidence in women treated with typical antipsychotics, 20 of 28 women who developed galactorrhea failed to spontaneously report this side effect on general inquiry by treating physician about medication side effects⁵⁴, so it is important to develop scales that let women comfortable to discuss sexuality.

This study had some limitations that should be considered when interpreting the data. First, all patients were recruited with ages ranging from 20 to 66 years. The sexual dysfunction worsens with age since 39% of

40-year-olds have some degree of erectile dysfunction (5% are completely impotent), but by the age of 70, two thirds have some degree of erectile dysfunction and complete impotence triples to 15%⁵⁵. Second, in this study there were no exclusion criteria such as comorbid depressive syndrome or diabetes, treatment with antidepressants, use of alcohol or cigarette smoking, and thyroid problems. This is not a longitudinal study, and there were no measurements of the effects of the illness on sexual functioning prior to medication treatment. Since this is a cross-sectional study, sexual dysfunction was evaluated at a single time point during the patients' drug therapy and no baseline sexual dysfunction was determined; therefore, there was no distinction between drug-induced or other causative factors. Because of the small sample size it was not possible to draw conclusions regarding cause and effects and possible relationship of antipsychotic doses. However, it is known that the side effects of certain drugs are drug-dependent⁴².

Schizophrenic patients have a certain level of sexual life that cannot be ignored by physicians. When patients are stable, they want to maintain their sexual life. Because of the high rates of sexual dysfunction, psychiatrists should pay more attention and ask specific questions about their patients' sexual life in routine clinical practice. Structured scales can be useful to diminish the embarrassment and discomfort for patients and physicians when this issue is raised. Controlled studies should directly inquire about sexual side effects and investigate how such side effects alter medication compliance and quality of life. The development of reliable and valid detailed side effect rating scales for use in research trials and in clinical encounters, such as the ASEX and DGSFi, should help to further elucidate data on sexual side effects⁵³. A study showed that the prevalence of sexual dysfunction associated with quetiapine or risperidone was 11.7% based on spontaneous reports, but increased to 32% when assessed using a semi-structured interview³⁴. Thus, use of structured scales can yield a higher incidence of sexual dysfunction. There is a need of studies on multifactorial etiology of sexual dysfunction. Studies need to account for individual variation in what constitutes normal sexual functioning and confounding factors that can affect sexual functioning². These include differences between genders, alcohol and tobacco use, relationship difficulties, co-prescribed medications and other clinical or psychiatric symptoms. Sexual dysfunctions are different between males and females with schizophrenia and further research on this area should be conducted to clarify this complex subject. This study showed that the combination of medications (two or more kinds of antipsychotics and antidepressants) leads to high rates of sexual dysfunctions; therefore, trying to use antipsychotic in monotherapy or lower doses, whenever possible, would be of great benefit to the patient in terms of achieving a healthier sexual life.

Since sexual dysfunction has high prevalence in patients with schizophrenia spectrum, psychiatrists' awareness and sensitivity regarding this important side effect and choosing the correct treatment would contribute to a better quality of life for these patients.

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References

- Falkai P, Wobrock T, Lieberman J, Glenthøj B, Gattaz WF, Möller HJ. Diretrizes da Federação Mundial das Sociedades de Psiquiatria Biológica para o tratamento biológico da esquizofrenia. Parte 2: tratamento de longo prazo. *Rev Psiq Clín.* 2006;33(Suppl 1):65-100.
- Haddad PM, Sharma SG. Adverse effects of atypical antipsychotics: differential risk and clinical implications. *CNS Drugs.* 2007;21(11):911-36.
- Aizenberg D, Zemishlany Z, Dorfman-Etrog P, Weizman A. Sexual dysfunction in male schizophrenic patients. *J Clin Psychiatry.* 1995;56(4):137-41.
- Wesby R, Bullimore E, Earle J, Heavey A. A survey of psychosexual arousability in male patients on depot neuroleptic medication. *Eur Psychiatry.* 1996;11:81-6.
- Wallace M. Real progress – the patient's perspective. *Int Clin Psychopharmacol.* 2001;16 Suppl 1:S21-4.
- Olsson M, Uttaro T, Carson WH, Tafesse E. Male sexual dysfunction and quality of life in schizophrenia. *J Clin Psychiatry.* 2005;66(3):331-8.
- Zemishlany Z, Weizman A. The impact of mental illness on sexual dysfunction. *Adv Psychosom Med.* 2008;29:89-106.
- Plevin D, Galletly C, Roughan P. Sexual dysfunction in men treated with depot antipsychotic drugs: a pilot study. *Sex Health.* 2007;4(4):269-71.
- Kotin J, Wilbert DE, Verburg D, Soldinger SM. Thioridazine and sexual dysfunction. *Am J Psychiatry.* 1976;133(1):82-5.
- Mitchell JE, Popkin MK. Antipsychotic drug therapy and sexual dysfunction in men. *Am J Psychiatry.* 1982;139(5):633-7.
- Üçok A, Incesu C, Aker T, Erkoç S. Sexual dysfunction in patients with schizophrenia on antipsychotic medication. *Eur Psychiatry.* 2007;22(5):328-33.
- Peuskens J. Prolactin elevation and sexual dysfunction. In: Peuskens J, editor. A literature review of "prolactin in schizophrenia". Clear perspectives: management issues in schizophrenia. 1997;1(3):17-27.
- Kasperek-Zimowska B, Brodniak WA, Sarol-Kulka A. Sexual disorders in schizophrenia – overview of research literature. *Psychiatr Pol.* 2008;42(1):97-104.
- Haro JM, Salvador-Carulla L. The SOHO (Schizophrenia Outpatient Health Outcome) study: implications for the treatment of schizophrenia. *CNS Drugs.* 2006;20(4):293-301.
- Macdonald S, Halliday J, MacEwan T, et al. Nithsdale Schizophrenia Surveys 24: sexual dysfunction. Case-control study. *Br J Psychiatry.* 2003;182:50-6.
- Konarzewska B, Szulc A, Popławska R, Galiska B, Juchnowicz D. [Impact of neuroleptic-induced hyperprolactinemia on sexual dysfunction in male schizophrenic patients]. *Psychiatr Pol.* 2008;42(1):87-95.
- Ghadirian AM, Chouinard G, Annable L. Sexual dysfunction and plasma prolactin levels in neuroleptic-treated schizophrenic outpatients. *J Nerv Ment Dis.* 1982;170(8):463-7.
- Meston CM, Gorzalka BB. Psychoactive drugs and human sexual behavior: the role of serotonergic activity. *J Psychoactive Drugs.* 1992;24(1):1-40.
- Petty RG. Prolactin and antipsychotic medications: mechanisms of action. *Schizophr Res.* 1999;35(Suppl):S67-73.

20. Rosenberg KP, Bleiberg KL, Kosci J, Gross C. A survey of sexual side effects among severely mental ill patients taking psychotropic medication: impact on compliance. *J Sex Marital Ther.* 2003;29(4):289-96.
21. Rosa MA, Elkis H. Adesão em esquizofrenia. *Rev Psiq Clín.* 2007;34 Suppl 2:189-92.
22. Lambert M, Conus P, Eide P, et al. Impact of present and past antipsychotic side effects on attitude toward typical antipsychotic treatment and adherence. *Eur Psychiatry.* 2004;19(7):415-22.
23. Finn SE, Bailey JM, Schultz RT, Faber R. Subjective utility ratings of neuroleptics in treating schizophrenia. *Psychol Med.* 1990;20(4):843-8.
24. Dickson RA, Glazer W. Development of a scale to assess sexual functioning. Programs and abstracts from the 153rd Annual American Psychiatric Association Meeting. Chicago, Illinois; 2000.
25. McGahuey CA, Gelemborg AJ, Laukes CA, Moreno FA, Delgado PI, McKnight KM, Manber R. The Arizona Sexual Experience Scale (ASEX): reliability and validity. *J Sex Marital Ther.* 2000;26(1):25-40.
26. Montejo AL, Rico-Villademoros F. Psychometric properties of the Psychotropic-Related Sexual Dysfunction Questionnaire (PRSexDQ-SALSEX) in patients with schizophrenia and other psychotic disorders. *J Sex Marital Ther.* 2008;34(3):227-39.
27. Reynolds CF 3rd, Frank E, Thase ME, Houck PR, Jennings JR, Howell JR, et al. Assessment of sexual function in depressed, impotent, and healthy men: factor analysis of a Brief Sexual Function Questionnaire for men. *Psychiatry Res.* 1998;24(3):231-25.
28. Byerly M, Nakonezny P, Fisher R, Magouirk B, Rush AJ. An empirical evaluation of the Arizona sexual experience scale and a simple one-item screening test for assessing antipsychotic-related sexual dysfunction in outpatients with schizophrenia and schizoaffective disorder. *Schizophr Res.* 2006;81(2-3):311-6.
29. Dossenbach M, Hodge A, Anders M, Molnár B, Peciukaitiene D, Krupka-Matuszczyk I, et al. Prevalence of sexual dysfunction in patients with schizophrenia: international variation and underestimation. *Int J Neuropsychopharmacol.* 2005;8(2):195-201.
30. Costa AM, Lima MS, Faria M, Filho SR, Oliveira IR, Mari JJ. A naturalistic, 9-month follow-up, comparing olanzapine and conventional antipsychotics on sexual function and hormonal profile for males with schizophrenia. *J Psychopharmacol.* 2006; May 19.
31. Soykan A. The reliability and validity of Arizona sexual experiences scale in Turkish ESRD patients undergoing hemodialysis. *Int J Impot Res.* 2004;16(6):531-4.
32. Smith SM, O'Keane V, Murray R. Sexual dysfunction in patients taking conventional antipsychotics medication. *Br J Psychiatry.* 2002;181:49-55.
33. Atmaca M, Kuloglu M, Tezcan E. A new atypical antipsychotic: quetiapine-induced sexual dysfunctions. *Int J Impot Res.* 2005;17(2):201-3.
34. Knegtering R, Castelein S, Bous H, Van Der Linde J, Bruggeman R, Kluijter H, et al. A randomized open-label study of the impact of quetiapine versus risperidone on sexual functioning. *J Clin Psychopharmacol.* 2004;24(1):56-61.
35. Teusch L, Scherbaum N, Böhme H, Bender S, Eschmann-Mehl G, Gastpar M. Different patterns of sexual dysfunctions associated with psychiatric disorders and psychopharmacological treatment. Results of an investigation by semistructured interview of schizophrenic and neurotic patients and methadone-substituted opiate addicts. *Pharmacopsychiatry.* 1995;28(3):84-92.
36. Abdo C, Fleury HJ. Aspectos diagnósticos e terapêuticos das disfunções sexuais femininas. *Rev Psiq Clín.* 2006;33(3):162-7.
37. Peuskens J, Sienaert P, De Hert M. Sexual dysfunction: the unspoken side-effects of antipsychotics. *Eur Psychiatry.* 1998;13 Suppl 1:23-30.
38. Volavka J, Czobor P, Cooper TB, Sheitman B, Lindenmayer JP, Citrome L, et al. Prolactin levels in schizophrenia and schizoaffective disorders patients treated with clozapine, olanzapine, risperidone, or haloperidol. *J Clin Psychiatry.* 2004;65(1):57-61.
39. Aizenberg D, Modai I, Landa A, Gil-Ad I, Weizman A. Comparison of sexual dysfunction in male schizophrenic patients maintained on treatment with classical antipsychotics versus clozapine. *J Clin Psychiatry.* 2001;62(7):541-4.
40. Cutler AJ. Sexual dysfunction and antipsychotic treatment. *Psychoneuroendocrinology.* 2003;28 Suppl 1:69-82.
41. Lambert M, Haro JM, Novick D, Edgell ET, Kennedy L, Ratcliffe M, et al. Olanzapine vs. other antipsychotics in actual out-patient settings: six months tolerability results from the European Schizophrenia Out-patient Health Outcomes study. *Acta Psychiatr Scand.* 2005;111(3):232-43.
42. Bobes J, Garc A-Portilla MP, Rejas J, et al. Frequency of sexual dysfunction and other reproductive side-effects in patients with schizophrenia treated with risperidone, olanzapine, quetiapine, or haloperidol: the results of the EIRE study. *J Sex Marital Ther.* 2003;29(2):125-47.
43. Montejo González AL, Rico-Villademoros F, Tafalla M, et al. A 6-month prospective observational study on the effects of quetiapine on sexual functioning. *J Clinical Psychopharmacol.* 2005;25(6):533-8.
44. Kelly DL, Conley RR. A randomized double-blind 12-week study of quetiapine, risperidone or fluphenazine on sexual functioning in people with schizophrenia. *Psychoneuroendocrinology.* 2006;31(3):340-6.
45. Westheide J, Cohen S, Bender S, Cooper-Mahkorn D, Erfurth A, et al. Sexual dysfunction in psychiatric inpatients: the role of antipsychotic medication. *Pharmacopsychiatry.* 2007;40(4):140-5.
46. Breier AF, Malhotra AK, Su TP, et al. Clozapine and risperidone in chronic schizophrenia: effects on symptoms, parkinsonian side effects, and neuroendocrine response. *Am J Psychiatry.* 1999;156(2):294-8.
47. Hummer M, Kemmler G, Kurz M, et al. Sexual disturbances during clozapine and haloperidol treatment for schizophrenia. *Am J Psychiatry.* 1999;156(4):631-3.
48. Crawford AM, Beasley CM Jr, Tollefson GD. The acute and long-term effect of olanzapine compared with placebo and haloperidol on serum prolactin concentrations. *Schizophr Res.* 1997;26(1):41-54.
49. David SR, Taylor CC, Kinon BJ, Breier A. The effects of olanzapine, risperidone, and haloperidol on plasma prolactin levels in patients with schizophrenia. *Clin Ther.* 2000;22(9):1085-96.
50. Kleinberg DL, Davis JM, de Coster R, et al. Prolactin levels and adverse events in patients treated with risperidone. *J Clin Psychopharmacol.* 1999;19(1):57-61.
51. Perkins DO. Prolactin- and endocrine-related disorders in schizophrenia. In: Meyer JM, Nasrallah HA, editores. *Medical illness and schizophrenia.* Washington DC/London: American Psychiatric Publishing, Inc.; 2003. p. 215-27.
52. Peuskens J, Link CG. A comparison of quetiapine and chlorpromazine in the treatment of schizophrenia. *Acta Psychiatry Scand.* 1997;96(4):265-73.
53. Compton MT, Miller AH. Sexual side effects associated with conventional and atypical antipsychotics. *Psychopharmacol Bull.* 2001;35(3):89-108.
54. Windgassen K, Wesselmann U, Schulze Mönking H, et al. Galactorrhea and hyperprolactinemia in schizophrenic patients on neuroleptics: frequency and etiology. *Neuropsychobiology.* 1996;33(3):142-6.
55. Stahl S. Stahl's essential psychopharmacology. In: Stahl S, editor. *Neuroscientific basis and practical applications.* 3rd ed. Cambridge: Cambridge University Press; 2008. p. 999.