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Original Research

Depression, selective serotonin reuptake inhibitors, and sexual wellbeing in assigned females: exploring the moderating role of sexual flexibility

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Abstract

Background: Depression often causes sexual dysfunction, including reduced desire and pleasure, and selective serotonin reuptake inhibitors (SSRIs), commonly used to treat depression, can worsen these issues, leading to treatment discontinuation.
Aim: To examine sexual wellbeing differences across depression and SSRI groups, how depression, SSRI use, and sexual flexibility predict sexual outcomes, and whether sexual flexibility moderates the relationship between sexual functioning, distress, and pleasure.
Methods: Participants ($N = 357$, mean age 26.8 years) assigned female sex at birth were recruited for an online cross-sectional study. Participants were grouped by SSRI use and depression severity: SSRIs-low depression ($n = 86$), SSRIs-high depression ($n = 117$), no SSRIs-low depression ($n = 81$), and no SSRIs-high depression ($n = 73$).
Outcomes: Validated measures of depression, sexual function, sexual distress, sexual flexibility, and sexual pleasure were used.
Results: Analyses of variance (ANOVAs) and multiple regressions examined relationships between depression, SSRI use, and sexual wellbeing. Moderation analyses tested whether sexual flexibility moderated the link between sexual functioning, distress, and pleasure. The SSRIs-high depression group reported the poorest sexual wellbeing, while the No SSRIs-low depression group reported the highest. Depression and SSRI use predicted increased sexual distress and decreased functioning, pleasure, and flexibility, explaining 21%-26% of variance. Sexual flexibility moderated the relationship between functioning and pleasure, with stronger effects at lower flexibility levels.
Clinical Implications: Sexual flexibility may improve sexual functioning and pleasure, providing a positive, adaptable framework for therapy; thus, psychosexual and educational interventions focusing on flexibility could enhance sexual pleasure and reduce distress, fostering sexual resilience and improving relationship dynamics.
Strengths and Limitations: Strengths include a nuanced analysis of depression severity and SSRI use, offering a comprehensive view of sexual wellbeing. Limitations include reliance on self-reported medication use, inability to assess specific SSRIs, and potential confounding from concurrent antidepressant use.
Conclusion: SSRIs and depression each uniquely affect sexual functioning, distress, and pleasure, such that those with moderate to severe depression and SSRI use report significantly poorer sexual outcomes.

Keywords: depression; antidepressant; sexual dysfunction; sexual flexibility; iatrogenic sexual dysfunction; SSRI.

Introduction

Depression is the leading cause of illness and disability, afflicting 280 million people worldwide.[1] It is twice as common in women and is characterized by persistent sadness, anhedonia, and a range of physical and cognitive symptoms, resulting in significant impairment in daily functioning and quality of life.[1] Depression can be thought of as both a continuum of symptoms ("depression symptoms"), or as a diagnostic category (eg, major depressive disorder (MDD), a mood disorder that causes a persistent feeling of sadness and loss of interest [DSM-5-TR]).[2] A frequently cited symptom of depression is sexual dysfunction[3]; indeed, a key diagnostic criterion for MDD is loss of pleasure, which can include diminished interest or pleasure in sex.[2]

Adding complexity to this picture, the first line treatment for depression, selective serotonin reuptake inhibitors (SSRIs),[4] are also associated with significant sexual functioning concerns. Despite being the most widely prescribed antidepressant class, rates of sexual dysfunction are considerably higher with SSRI treatment compared to other classes of antidepressants, indicating that SSRIs are differentially associated with sexual dysfunction.[5] Sexual side effects have significant implications for patient outcomes; SSRI-related sexual difficulties are a leading cause of antidepressant discontinuation.[6] Although sexual functioning is important to the majority of patients with depression undergoing antidepressant therapy, much remains unknown about how SSRIs and depression uniquely contribute to sexual issues.[5]

The relationship between depression and sexual dysfunction is bidirectional, with SSRI treatment adding further complexity to the relationship. Depression in women is associated with decreased arousal,[7] reduced desire for, and interest in, sex,[8] orgasmic difficulties,[9] and sexual pain.[10] Untreated

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depression increases baseline sexual dysfunction, which SSRIs can exacerbate.[11] Research shows that although both depression and antidepressants impact sexual desire, physiological changes such as orgasm and arousal difficulties are primarily linked to antidepressant use.[12-15] This pattern of findings suggests that SSRIs may cause additional, unique sexual side effects above and beyond those associated with depression.

SSRIs and depression appear to have both distinct and overlapping impacts on sexual dysfunction,[16] complicating the identification of unique contributing factors. Moreover, evaluating broader dimensions of sexual wellbeing, such as sexual distress and pleasure is essential to ensure a more comprehensive understanding of sexual wellbeing not captured by commonly used measures of sexual function that focus on aspects such as desire, arousal, and orgasm. Sexual distress, defined as negative emotional responses (eg, worry, anxiety, frustration, bother, feelings of inadequacy)[17] associated with sexual function and experiences, can affect one's overall quality of life, relationships, and mental health, even if physiological aspects of sexual function are intact.[18] Similarly, sexual pleasure, defined as a sense of wellbeing derived from the experience of being sexual (including positive feelings of satisfaction, excitement, love, and romance)[19,20] plays a key role in sexual wellbeing, contributing to satisfaction and fulfillment.

There is a growing understanding of the psychological and social factors that moderate the relationship between sexual dysfunction and sexual distress and pleasure, one of which is sexual flexibility. Sexual functioning issues (eg, pain with penetration, low desire, lubrication issues) can disrupt individuals' intended sexual experiences and may require flexibility in trying alternative strategies to alter sexual scripts—cognitive schemata that operate on cultural, interpersonal, and intrapersonal levels to guide expectations about sexual behavior and dictate a sequence of generally predictable behaviors.[21] Greater sexual flexibility, marked by less rigid thoughts and behaviors, is linked to better coping strategies and positive psychosexual outcomes, such as increased satisfaction and reduced distress.[22] Sexually flexible individuals who are able to change the way they think about sex or change their behavioral approach to sexual activity are thought to cope better with acute and chronic sexual issues[22,23]; suggesting sexual flexibility may be a promising treatment target for individuals with sexual difficulties related to depression and SSRI use. Unique considerations for SSRI use and depression, such as cognitive flexibility (the ability to adapt cognitive processing strategies to face new and unexpected conditions in the environment),[24] which is found to be impacted in individuals experiencing depression),[25] suggest the need for study specifically within this population. It is not yet known whether sexual flexibility moderates the relationship between dysfunction and distress or pleasure in samples experiencing depression symptoms and SSRI use. Investigating this relationship could provide a valuable treatment target to support individuals experiencing SSRI and depression-related sexual dysfunction.

The present study focused on female assigned individuals and examined how depression symptoms and SSRI medications uniquely impact sexual wellbeing and the influence of sexual flexibility on these relationships through the following research questions:

1. *How do sexual wellbeing outcomes (sexual functioning, distress, pleasure, and flexibility) differ across groups of participants with high vs. low levels of depression symptoms, using SSRIs vs. not?* We hypothesized that the groups using SSRIs and those with moderate to high depression symptoms would report significantly poorer sexual wellbeing outcomes than the groups with low depression symptoms and no SSRI use. Furthermore, participants with moderate to high depression symptoms *and* current SSRI use would report the poorest outcomes due to the combined effects of the physiological effects of SSRIs (eg, genital numbness) and psychological effects (eg, anhedonia) of depression, based on previous research using a sample of patients with a diagnosis of MDD.[26]
2. *Do depression symptoms, SSRI use, and sexual flexibility predict sexual wellbeing outcomes?* We hypothesized that greater depression symptoms and SSRI use would each significantly predict poor sexual wellbeing outcomes, as previous research has suggested that depression and SSRIs may uniquely impact sexual wellbeing.[12] We also expected that greater sexual flexibility would predict more positive sexual wellbeing outcomes.
3. *Does sexual flexibility moderate the relationship between participants' (1) sexual functioning and sexual distress and (2) sexual functioning and sexual pleasure?* Given that sexual flexibility is associated with improved ability to navigate sexual difficulties,[22] we hypothesize that sexual flexibility would moderate the relationship between sexual functioning and sexual distress (model 1) and sexual functioning and sexual pleasure (model 2). Specifically, we hypothesized that individuals lower in sexual flexibility would have a larger negative association between sexual functioning and sexual distress, as well as a larger positive sexual functioning and sexual pleasure.

Methods

Participants

Inclusion criteria were: female sex assigned at birth (defined by self-reported genital anatomy, as questionnaires were specific to genitals [ie, Female Sexual Function Index (FSFI)][27] with any gender identity, ≥ 18 years of age, fluent in English. Exclusion criteria were: discontinued SSRI use to control for potential after-effects (eg, post-SSRI sexual dysfunction)[28,29] and male sex assigned at birth. We sampled for participants who both did and did not have experience of using SSRIs for depression symptoms and who experienced a range of depression symptoms from mild through to severe.

Participants were assigned to one of four groups based on their level of depression symptoms using established cut-off values (Beck Depression Inventory, second edition [BDI-II], see Methods below)[30] and SSRI status:

1. *SSRIs-low depression*: current SSRI use, BDI-II score ≤ 19
2. *SSRIs-high depression*: current SSRI use, BDI-II score ≥ 20
3. *No SSRIs-low depression*: never used SSRI medication, BDI-II score ≤ 19
4. *No SSRIs-high depression:* never used SSRI medication, BDI-II score ≥ 20.

Measures

Demographics

Demographic questions included age, educational attainment, occupational status, religion, place of birth, income, and relationship status.

Mood symptoms and SSRI use

Depression

The BDI-II[31] is a 21-item self-report measure of depression symptoms over the previous 2 weeks. Higher total scores reflective of greater depression symptom severity. The BDI-II has excellent internal consistency and validity.[31] In the present study, Cronbach's $\alpha = .92$. Previous research has established cut-off scores to indicate depression symptom severity where: 0-13 is minimal, 14-19 is mild, 20-28 is moderate, and 29-63 is severe,[32] which was used to define group membership in the present sample where <19 = low depression and > 20 = high depression.

SSRI Use

Participants were asked if they currently, or have ever, taken selective serotonin reuptake inhibitors (SSRIs). The names of common SSRI medications were provided in a list. Responses were used to define group membership in the sample: (1) currently using SSRI medication (SSRI group), (2) previous but not current (discontinued) use of SSRI medication, and (3) never used SSRI medication (No SSRI group). Participants in the discontinued use group were excluded from the present analysis.

Sexual functioning and wellbeing

Sexual Functioning - Female Sexual Functioning Index

The FSFI[28] is a 19-item self-report questionnaire assessing sexual function over the past four weeks across six domains: lubrication, arousal, desire, pain, orgasm, and satisfaction. Higher scores indicate greater functioning. It is a reliable measure, with clinical and psychometric validity.[27] The FSFI has shown discriminant validity between women with and without sexual complaints, with a total cutoff score for sexual dysfunction of 26.55.[33] In the present study, Cronbach's $\alpha = .93$.

Sexual Distress - Sexual Distress Scale

The Sexual Distress-Sexual Distress Scale is a 5-item self-report scale assessing frequency of sexual distress in the past four weeks, with excellent reliability.[34] Higher scores indicate greater distress. In the present study, Cronbach's $\alpha = .92$.

Sexual Flexibility – SexFlex Scale

Participants completed the SexFlex Scale[22] to assess sexual script flexibility during experiences of sexual difficulty. Higher scores indicate greater flexibility. The SFS demonstrates good convergent and discriminant validity, and high internal consistency.[22] In the present study, Cronbach's $\alpha = .91$.

Sexual Pleasure - Sexual Pleasure Scale

The Sexual Pleasure Scale[36] is a 3-item scale assessing the extent of sexual pleasure that participants experienced from their sex life in the past 4 weeks. Higher scores indicate greater sexual pleasure. The SPS has good psychometric qualities and reliability as well as high internal consistency in past studies.[35] In the present study, Cronbach's $\alpha = .92$.

Procedures

Participants were recruited through social media posts (ie, Facebook, Twitter, Instagram, and Reddit), and posters in the local community. Recruitment occurred between May 2020 and February 2021. The survey was hosted on Qualtrics online survey software (Provo, Utah). The first page of the survey included the study information and consent form. After providing consent, participants continued onto the rest of the questionnaires. All responses to the survey were anonymous. The survey took up to 45 minutes to complete and concluded with a debriefing form. For compensation, participants were directed to a separate survey, in order to preserve their anonymity, and had the option to enter their email address into a prize draw for 1 of 20 $25 (CAD) Amazon gift cards. This study received ethical clearance from the Queen's University General Research Ethics Board.

Data considerations

Data were examined for normality (via visualization of data and Shapiro–Wilk test) and outliers where appropriate. No missing data were imputed. A series of ANOVAs, Chi-squared tests of independence, and multiple regressions were undertaken to understand the relationships among depression symptoms, SSRI use, and sexual wellbeing outcomes. Effect sizes are presented as partial eta squared (η^2).[36] If ANOVAs were significant, Tukey's least significant difference (LSD) post hoc tests (variances equal) and Games-Howell (variances unequal) were implemented to determine group differences. Finally, a moderation analysis, using PROCESS[37] Model 1 was undertaken to examine whether levels of sexual flexibility moderate the relationship between sexual functioning and sexual distress/pleasure. Analyses were conducted using SPSS (Chicago, Illinois) Version 29.0.2. Alpha values (2-tailed) were set at $P < .05$. G*Power version 3.1 (Faul et al., 2007) indicated that a sample of $n = 280$ was required for ANOVAs with 4 groups (chosen due to highest sample size requirement), 80% power, and a hypothesized moderate effect size.[38]

Results

Sample characteristics

A total of 425 participants completed the survey. Ineligible participants ($n = 63$, Figure 1) were excluded, and the remaining individuals ($n = 357$) were assigned to one of four groups based on their level of BDI-II depression symptoms using established cut-off values: *SSRIs-low depression*: current SSRI use, BDI-II score ≤ 19 ($n = 86$); *SSRIs-high depression*: current SSRI use, BDI-II score ≥ 20 ($n = 117$); *no SSRIs-low depression*: never used SSRI medication, BDI-II score ≤ 19 ($n = 81$); *and no SSRIs-high depression:* never used SSRI medication, BDI-II score ≥ 20 ($n = 73$).

Participants were on average 26.79 years old ($SD = 7.74$ years). The majority of participants were highly educated, non-religious, heterosexual, Caucasian, born in North America, and in a relationship. A significantly larger proportion of individuals with moderate to high levels of depression symptoms reported lower household income. There were no other significant group differences on demographics (Table 1).

Group comparisons on sexual wellbeing outcomes

Across all sexual wellbeing measures (sexual function, distress, flexibility, and pleasure), the SSRIs-high depression group reported the poorest outcomes, while the No SSRIs-low depression group reported the best outcomes (Table 2). The pattern of results was the same for sexual dysfunction,

Table 1. Group Comparison of Sample Characteristics and Demographics.

	Total Sample M (SD)	SSRIs-low depression M (SD)	SSRIs-high depression M (SD)	No SSRIs-low depression M (SD)	No SSRIs-high depression M (SD)	Test statistic *F*	P value P value	Effect Size η^2
Age	26.79 (7.74)	25.43 (5.92)	27.56 (8.11)	27.76 (9.18)	26.68 (8.33)	1.58	.195	.01
BDI-II	21.91	10.50 (5.00)	32.87 (9.33)	8.49 (5.93)	32.68 (9.78)	259.16	<.001	.69
	% (N)	% (N)	% (N)	% (N)	% (N)	X^2	P value	Cramer's V
Gender						6.07	.415	.09
Genderqueer	0.6% (2)	1.2% (2)	0.0% (0)	0.0% (0)	1.4% (1)			
Non-Binary	2.5 (9)	2.4% (2)	4.3% (5)	0.0% (0)	2.7% (2)			
Woman	96.9% (344)	96.5% (82)	95.7% (112)	100.0% (80)	95.9% (70)			
Ethnicity						16.97	.713	.13
Black	3.3% (11)	4.9% (4)	2.7% (3)	4.1% (3)	1.6% (1)			
Indigenous	0.9% (3)	1.2% (1)	0.9% (1)	0.0% (0)	1.6% (1)			
Latina/o/x/e	0.9% (3)	7.3% (6)	6.3% (7)	6.8% (5)	6.3% (4)			
Other	0.6% (2)	0.0% (0)	0.9% (1)	0.0% (0)	1.6% (1)			
South Asian	1.5% (5)	0.0% (0)	2.7% (3)	2.7% (2)	0.0% (0)			
Southeast Asian	5.1% (17)	0.0% (0)	0.9% (1)	1.4% (1)	1.6% (1)			
White	81.0% (269)	85.4% (70)	81.3% (91)	79.7% (59)	76.6% (49)			
Place of Birth						36.83	.098	.19
Africa	1.7% (6)	1.2% (1)	0.9% (1)	3.8% (3)	1.4% (1)			
Asia	3.1% (11)	0.0% (0)	5.1% (6)	3.8% (3)	2.8% (2)			
Australia	2.5% (9)	1.2% (1)	3.4% (4)	3.8% (3)	1.4% (1)			
Canada	31.0% (110)	34.9% (30)	28.2% (33)	31.3% (25)	30.6% (22)			
Eastern Europe	1.7% (6)	0.0% (0)	0.0% (0)	6.3% (5)	1.4% (1)			
Latin/South America	2.0% (7)	3.5% (3)	0.9% (1)	2.5% (2)	1.4% (1)			
Middle East	0.8% (3)	0.0% (0)	1.7% (2)	0.0% (0)	1.4% (1)			
Other	3.1% (11)	4.7% (4)	1.7% (2)	3.8% (3)	2.8% (2)			
United States	41.7% (148)	48.8% (42)	44.4% (52)	31.3% (35)	40.3% (29)			
Western Europe	12.4% (44)	5.8% (5)	13.7% (16)	13.8% (11)	16.7% (12)			
Education						34.16	.082	.18
Some high school	1.4% (5)	4.7% (4)	0.0% (0)	0.0% (0)	1.4% (1)			
High school graduate	8.1% (29)	10.5% (9)	7.7% (9)	11.1% (9)	2.8% (2)			
Some trade school	0.3% (1)	0.0% (0)	0.9% (1)	0.0% (0)	0.0% (0)			
Trade school graduate	1.7% (6)	0.0% (0)	0.9% (1)	0.0% (0)	0.0% (0)			
Some undergraduate	22.5% (80)	1.2% (1)	0.9% (1)	0.0% (0)	5.6% (4)			
Undergraduate graduate	34.3% (122)	20.9% (29)	26.5% (31)	16% (13)	25% (18)			
Some graduate school/professional school degree	9.6% (34)	11.6% (10)	6.8% (8)	11.1% (9)	38.9% (28)			
Graduate/professional school degree	19.9% (71)	17.4% (15)	23.1% (4)	23.5% (2)	13.9% (2)			
Other	2.2% (8)	0.0% (0)	3.4% (4)	2.5% (2)	2.8% (2)			

(*Continued*)

Table 1. Continued

	Total Sample M (SD)	SSRIs-low depression M (SD)	SSRIs-high depression M (SD)	No SSRIs-low depression M (SD)	No SSRIs-high depression M (SD)	Test statistic *F*	P value P value	Effect Size η^2
Religion						19.43	.079	.14
Catholic	26.1% (91)	23.8% (20)	22.8% (26)	29.9% (23)	30.1% (22)			
Jewish	2.6% (9)	3.6% (31)	0.0% (0)	3.9% (3)	4.1% (23)			
None	36.5% (127)	36.9% (12)	38.6% (44)	37.7% (29)	31.5% (18)			
Other	16.7% (58)	14.3% (84)	20.2% (114)	6.5% (5)	24.7% (73)			
Protestant	18.1% (63)	21.4% (18)	18.4% (21)	22.1% (17)	9.6% (7)			
Household Income						33.16	.016	.19
$0 - 19 999	23.1%(74)	12.8% (10)	31.1% (32)	14.9% (11)	32.3% (21)			
$20 000 - 39 000	17.2% (55)	16.7% (13)	14.6% (15)	18.9% (14)	20% (13)			
$40 000 - 59 000	15.9% (51)	14.1% (11)	17.5% (18)	23.0% (17)	7.7% (5)			
$60 000 - 79 000	13.1% (42)	15.4% (12)	11.7% (12)	10.8% (8)	15.4% (10)			
$80 000 - 99 000	9.1% (29)	11.5% (9)	3.9% (4)	8.1% (6)	15.4% (10)			
$100 000 - 119 999	7.2% (23)	7.7% (6)	8.7% (13)	8.1% (6)	3.1% (2)			
$120 000 +	14.4% (46)	21.8% (17)	12.6% (13)	16.2% (12)	6.2% (4)			
Occupational Status						19.31	.373	.14
Employed Full Time	33.2% (118)	38.4% (33)	34.2% (40)	36.3% (29)	22.2% (16)			
Employed Part Time	12.4% (44)	10.5% (9)	15.4% (18)	13.8% (11)	8.3% (6)			
Unemployed	14.1% (50)	10.5% (9)	17.1% (20)	10% (8)	18.1% (13)			
Retired	0.8% (3)	0.0% (0)	0.9% (1)	2.5% (2)	0.0% (0)			
Student	33.8% (120)	36.0% (31)	27.4% (32)	32.5% (26)	43.1% (31)			
On Disability	1.4% (5)	1.2% (1)	1.7% (2)	0.0% (0)	2.8% (2)			
Other	4.2% (15)	3.5% (3)	3.4% (4)	5% (4)	5.6% (4)			
Relationship Status						4.41	.220	.11
Partnered	69.6% (247)	73.3% (63)	76.5% (62)	76.5% (62)	63.9% (46)			
Unpartnered	30.4% (108)	26.7% (23)	34.5% (40)	23.5% (19)	36.1% (26)			
Sexual Orientation						15.71	.401	.12
Asexual	1.4% (5)	1.2% (4)	1.7% (5)	2.5% (3)	0.0% (0)			
Bisexual	25.5% (91)	31.4% (27)	27.4% (32)	12.3% (10)	30.1% (22)			
Gay/lesbian	4.5% (16)	5.8% (5)	3.4% (4)	2.5% (2)	6.8% (5)			
Heterosexual	59.1% (211)	52.3% (45)	57.3% (67)	72.8% (59)	54.8% (40)			
Other	3.9% (14)	4.7% (4)	4.3% (5)	3.7% (3)	2.7% (2)			
Queer	5.6% (20)	4.7% (4)	6.0% (7)	6.2% (5)	5.5% (4)			

Note: BDI-II = Beck Depression Inventory, second edition; SSRI = Selective Serotonin Reuptake Inhibitor.

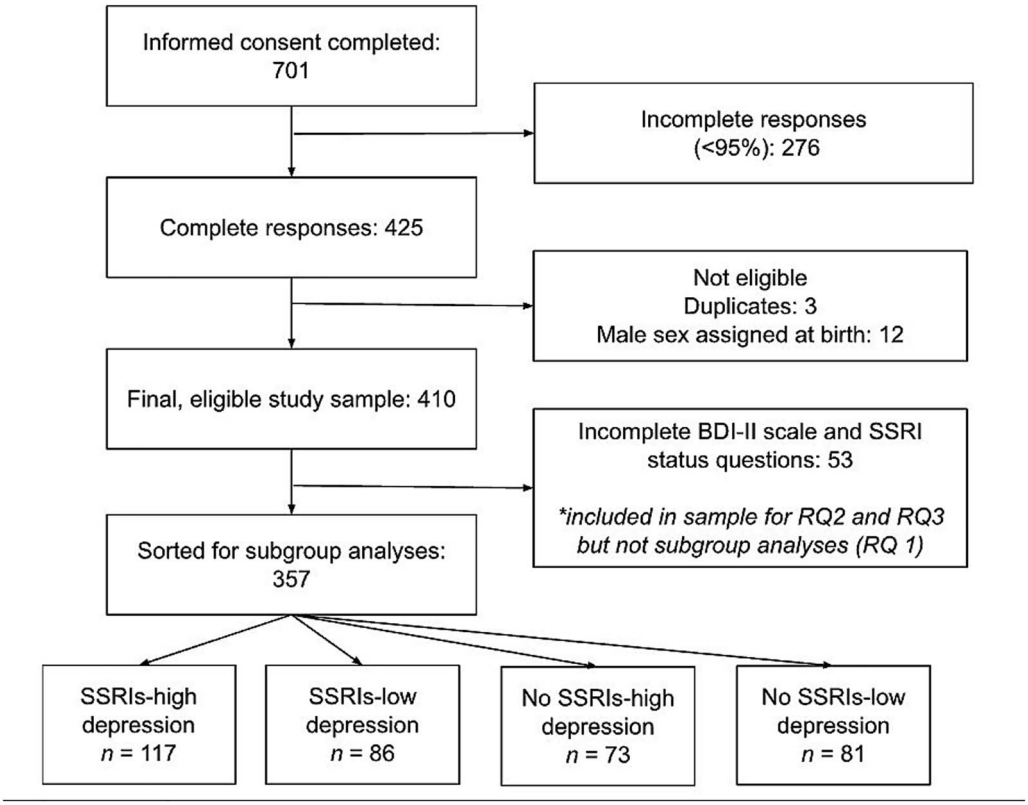

Figure 1. Flow chart illustrating the number of participants who completed each stage of the survey, and reasons for participant exclusion.
Note. BDI-II = Beck depression inventory, second edition; SSRI = selective serotonin reuptake inhibitor.

Table 2. Comparison of Mean Results Between Groups in Sexual Function, Distress, Flexibility, and Pleasure.

	SSRIs-low depression	SSRIs-high depression	No SSRIs-low depression	No SSRIs-high depression	*F*	*P* value	η^2
	M (SD)	M (SD)	M (SD)	M (SD)			
Sexual Function (FSFI)	24.00*† (7.04)	20.63* + (7.35)	27.78 + † ± (6.01)	22.53 ± (7.03)	14.70	< .001	.13
Sexual Distress (SDS)	7.67*† (5.08)	9.86* + (5.17)	5.32 + † ± (4.17)	8.86 ± (5.34)	14.02	< .001	.11
Sexual Flexibility (SexFlex)	15.19* (4.68)	13.77 + * (5.15)	16.74 + ± (4.60)	14.67 ± (4.74)	5.56	< .001	.05
Sexual Pleasure (SPS)	16.55*† (4.76)	14.16* + (5.31)	18.61 + † ± (3.41)	16.06 ± (4.96)	11.27	< .001	.11

Note. +† ±* indicate a significant post-hoc comparison.

distress, and pleasure. However, sexual flexibility scores between the two low-depression groups were not significant, indicating that use of SSRIs did not significantly influence sexual flexibility in these groups (Table 2). The average score for all groups, except the no SSRIs-low depression symptoms, fell below the clinical cut off on the FSFI (< 26.55),[33] indicating sexual dysfunction.

Associations among depression symptoms, SSRI use, and sexual wellbeing outcomes

Both depression symptoms and SSRI use (0 = no SSRIs, 1 = SSRI use) were positively correlated with greater sexual distress and negatively correlated with sexual functioning, pleasure, and flexibility (effect sizes ranging small to moderate, Table 3). Three multiple regression models examined unique contributions of SSRI use, depression symptoms (BDI-II), and sexual flexibility in predicting sexual wellbeing outcomes (dysfunction, distress, pleasure; Table 4). In all three models, depression symptoms, SSRI use, and sexual flexibility were each significant predictors of sexual dysfunction, sexual distress, and sexual pleasure.

Sexual flexibility as a moderator

Sexual distress model

A moderation analysis was conducted to examine whether sexual flexibility moderates the relationship between sexual functioning and sexual distress (Figure 2). Overall, the model was significant, and accounted for 41.3% of the variance in distress ($R^2 = 0.41$, $F(3, 311) = 72.96$, $P < .001$, $N = 315$). Sexual functioning ($b = -0.39$, $t(311) = -11.99$, $P \leq .001$) and sexual flexibility ($b = -0.16$, $t(311) = -3.24$, $P = .001$) were both significant predictors of sexual distress, where lower sexual functioning and sexual flexibility were associated with greater sexual distress. The interaction between functioning and flexibility was not significant ($b = 0.00$, $t(311) = 0.61$, $P = .545$), suggesting that sexual flexibility does not moderate the relationship between sexual functioning and sexual distress.

Sexual pleasure model

A second moderation analysis was conducted to examine whether sexual flexibility moderates the relationship between sexual functioning and sexual pleasure (Figure 3). The overall

Table 3. Correlation matrix: associations among variables.

Variable		Depression (BDI-II)	Sexual Function (FSFI)	Sexual Distress (SDS)	Sexual Flexibility (SexFlex)	Sexual Pleasure (SPS)	SSRI Status (dichotomous) 0 = Never 1 = Current
Depression (BDI-II)	Pearson's *r*	1	−.361**	.391**	−.217**	−.316**	.121*
	N	394	329	388	360	310	357
Sexual Function (FSFI)	Pearson's *r*		1	−.624**	.389**	.793**	−.212**
	N		339	337	316	286	308
Sexual Distress (SDS)	Pearson's *r*			1	−.360**	−.508**	.187**
	N			402	367	320	364
Sexual Flexibility (SexFlex)	Pearson's *r*				1	.479**	−.145**
	N				368	298	333
Sexual Pleasure (SPS)	Pearson's *r*					1	−.223**
	N					323	291
SSRI Status (dichotomous) 0 = Never 1 = Current	Pearson's *r*						1
	N						370

**Correlation is significant at the 0.01 level (2-tailed) *Correlation is significant at the 0.05 level (2-tailed) Note: BDI-II = Beck Depression Inventory, second edition; FSFI = Female Sexual Function Index; SexFlex = Sexual Flexibility Scale; SPS = Sexual Pleasure Scale; SSRI = Selective Serotonin Reuptake Inhibitors

Table 4. Multiple regression models examining the unique contributions of SSRI use, depression symptoms, and sexual flexibility in predicting sexual wellbeing outcomes.

Variable	Beta	t value	P value	R^2	Adjusted R^2
Model 1: Sexual Functioning (FSFI), *n* = 282					
SexFlex	.29	5.39	< .001	.22	.22
BDI	−.27	−5.03	< .001		
SSRI Status 0 = Never 1 = Current	−.14	−2.70	.007		
Model 2: Sexual Pleasure (SPS), *n* = 261					
SexFlex	.39	7.15	< .001	.26	.25
BDI	−.20	−3.55	< .001		
SSRI Status 0 = Never 1 = Current	−.15	−2.81	.005		
Model 3: Sexual Distress (SDS), *n* = 324					
SexFlex	−.25	−4.91	< .001	.22	.21
BDI	.32	6.29	< .001		
SSRI Status 0 = Never 1 = Current	.10	2.06	.040		

Note: BDI-II = Beck Depression Inventory, second edition; SSRI = Selective Serotonin Reuptake Inhibitor.

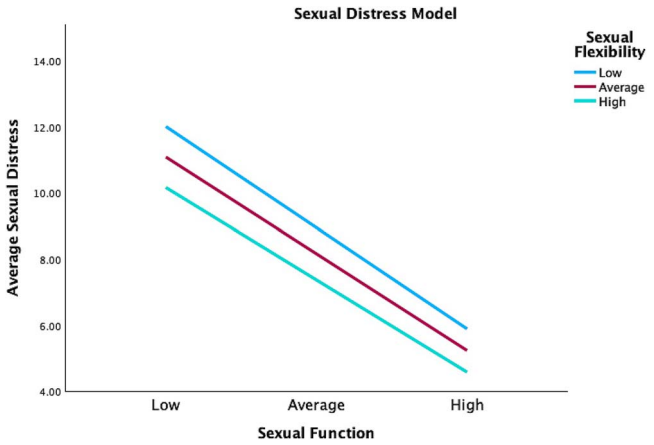

Figure 2. Linear relationship between sexual function and sexual distress as a function of sexual flexibility. Note. Main effect of sexual function (p = < .001).

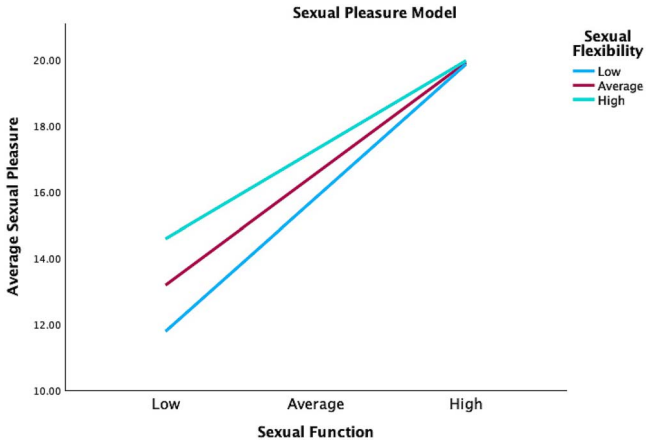

Figure 3. Sexual flexibility moderates the linear relationship between sexual function and sexual pleasure. Note. Main effect of sexual function (p = < .001) and moderating effect of sexual flexibility (p = < .001).

model was significant, and accounted for 66.7% of the variance in pleasure ($R^2 = 0.67$, $F(3, 263) = 175.64$, $P < .001$, $N = 267$). Sexual functioning ($b = 0.46$, $t(263) = 17.93$, $P \leq .001$) and sexual flexibility ($b = 0.15$, $t(263) = 3.90$, $P < .001$) were both significant predictors of sexual pleasure, where greater sexual functioning and sexual flexibility were associated with greater sexual pleasures. The interaction between functioning and flexibility was significant ($b = -0.02$, $t(263) = -3.99$, $P < .001$), indicating that sexual flexibility moderates the relationship between sexual functioning and sexual pleasure.

The conditional effects of sexual functioning on sexual pleasure were tested for low (−1 SD below the mean), average (mean), and high (+1 SD above the mean) levels of sexual flexibility. Each of the simple slope tests revealed a significant positive association between sexual functioning and sexual pleasure, but the largest association between sexual functioning and sexual pleasure was observed at low levels of sexual flexibility ($b = 0.55$, $t(263) = 17.10$, $P < .001$), as compared to moderate levels of sexual flexibility ($b = 0.46$, $t(263) = 17.93$, $P < .001$) and high levels of sexual flexibility, ($b = 0.36$, $t(263) = 10.05$, $P < .001$). There were no statistical significance transition points within the observed range of the moderator using the Johnson–Neyman method. Collectively, these results suggest that at lower levels of sexual flexibility, sexual functioning has a stronger, positive relationship with sexual pleasure, whereas at higher levels of sexual flexibility, the relationship remains positive and significant but weakens in magnitude.

Discussion

This study investigated how depression symptoms and SSRI medications uniquely impact sexual wellbeing and examined the influence of sexual flexibility, a potential treatment target, on these relationships. While past research has characterized SSRI-associated sexual dysfunction,[5-15] this study is the first to differentiate sexual wellbeing outcomes based on both depression severity and SSRI use in participants assigned female at birth, and the first to examine sexual flexibility in this context. Study findings align closely with broader literature,[5] confirming that depression and SSRI use are linked to greater distress and lower sexual functioning, pleasure, and flexibility.[5] This study's focus on the nuanced effects of SSRI use and depression severity offers critical insight, as past research often overlooked these compounding influences on sexual functioning.[11-15] Although past research identified a general trend of poorer sexual functioning with concurrent SSRI use and depression,[26] this study provides a new depth of analysis by parsing outcomes based on depression level. This study uniquely demonstrates that participants with high depression and SSRI use report significantly poorer sexual functioning compared to those with mild symptoms or no SSRI use—an analysis that, to our knowledge, is the first to differentiate outcomes by depression severity. These results underscore how the combined physiological effects of SSRIs and psychological impacts of depression can jointly exacerbate sexual dysfunction. Future research may further explore the effects of SSRIs and depression symptoms on sexual wellbeing outcomes through longitudinal designs.

Consistent with prior research,[13] the present study confirms that depression symptoms and SSRI use are unique predictors of sexual difficulties, with both factors contributing significantly to poorer sexual functioning and broader aspects of sexual wellbeing, including increased distress and decreased pleasure. Consideration of these broader markers of sexual wellbeing is critical for understanding the full impact of depression and SSRI treatment. In line with previous research highlighting sexual flexibility as a protective factor in managing sexual difficulties,[22] this study offers novel insights into sexual flexibility's role in sexual wellbeing. Although flexibility did not moderate the relationship between sexual functioning and sexual distress, it did significantly enhance sexual pleasure, suggesting a protective role in sexual experiences despite difficulties. This nuanced finding highlights the complexity of sexual wellbeing, as distress and pleasure may be influenced by different mechanisms. For example, when encountering sexual difficulties (eg, pain with penetration), distress (eg, related to anticipation of pain) may persist, but sexual flexibility may facilitate engagement in alternative activities that enhance pleasure. The study supports existing research showing that individuals with higher sexual flexibility tend to cope better with sexual functioning difficulties, displaying greater resilience in areas like sexual pleasure.[22,23] Notably, these findings are novel, marking the first examination of sexual flexibility within the context of SSRI-associated sexual dysfunction.

Research on sexual dysfunction often focuses on pathology and deficits, neglecting positive aspects of sexual experience, such as pleasure. Our study shifts this focus by exploring positive outcomes, even within the context of sexual difficulties related to SSRI use. We recognize that such dysfunction impacts areas of sexual wellbeing and quality of life beyond just function, including motivation for sexual activity and relationship dynamics. By using a positive psychology model, we aim to fill critical gaps in understanding what helps both patients and clinical communities thrive. This positive approach fosters a science of positive human flourishing, enhancing quality of life.[39] Adopting a holistic perspective that includes broader wellbeing measures like pleasure allows us to better understand the emotional and experiential components of sexual wellbeing, crucial for capturing the full impact of both depression and SSRI treatments.

This study's scope of analysis excluded individuals who are no longer using SSRIs in order to control for potential after-effects. However, it must be acknowledged that for individuals who experience SSRI-emergent sexual dysfunction, it is possible that sexual dysfunction will persist after *stopping* antidepressant treatment.[28] Post-SSRI Sexual Dysfunction (PSSD) is an iatrogenic condition of persistent sexual dysfunction following the discontinuation of SSRI/SNRI medication.[29] Despite a striking clinical manifestation, PSSD remains a highly under-recognized and unexplored phenomenon. Although this study did not look at PSSD, it has implications for enduring sexual dysfunction, as it is possible that some participants in this study cohort may go on to experience PSSD. Future research should examine sexual difficulties that persist beyond SSRI discontinuation.

The findings have significant clinical implications, particularly for individuals experiencing sexual wellbeing concerns related to depression and SSRI use. Beyond existing strategies for managing SSRI-emergent sexual difficulties that focus on drug type and dosage,[40] our findings suggest that enhancing sexual flexibility could be a promising target for sex therapy. Since flexibility is linked to increased sexual pleasure,

psychosexual interventions that focus on flexibility (eg, cognitive-behavioral therapy, CBT) offer a targeted approach to promote sexual pleasure in short-term counselling sessions, and educational materials can inform patients about flexibility and suggest ways to adopt a more adaptable approach to sex. It is recommended that interventions based on CBT to promote sexual flexibility be tested in clinical settings, prioritizing methods that address psychosocial and physiological aspects of sexual well-being.[23] Enhancing flexibility may be particularly beneficial for those struggling with the compounded effects of depression and SSRI treatment, potentially reducing the negative impact these factors have on psychosexual wellbeing and relationship dynamics. In addition, the use of longitudinal studies is essential in tracking changes over time, allowing for a more robust assessment of the impacts of SSRIs and depression on sexual well-being.

A key strength of this study is its investigation of the specific effects of SSRI use and depression symptoms on broader domains of sexual functioning, as well as the examination of psychological moderators. However, the study also has several limitations. First, we were unable to measure the effects of specific medications, despite literature suggesting that different SSRIs may have varying side effects[12]; the lack of specific analysis for different types of SSRIs limits detailed understanding of their differential effects. The reliance on self-reported medication use introduces potential inaccuracies, as participants may not always know the exact type of medication or dosage they are using. To ensure ecological validity, participants could report using multiple different SSRIs over time, appreciating that one might try different medications in the course of their treatments. All participants were currently using an SSRI, as per the eligibility criteria, though some participants reported additionally or previously using another type of antidepressant (eg, SNRI, atypical, and tricyclic). Considerations around sample diversity and generalizability should be noted, as these factors may affect the broader applicability of our findings. Finally, the sample was based on cross-sectional, self-reported data, which introduces bias and limits our ability to draw causal conclusions about the relationships observed.

Conclusions

SSRIs and depression have unique contributions to sexual functioning, sexual distress and pleasure. Assigned females using SSRIs and experiencing moderate to high depression symptoms experience significantly worse outcomes. Sexual flexibility is associated with lower distress and greater sexual pleasure and sexual functioning, and therefore, may be a target for interventions to support people coping with sexual difficulties secondary to SSRI use and/or depression symptoms. In addition, the cross-sectional nature of the study and the reliance on self-reported data, particularly regarding SSRI use, limit the generalizability and causal interpretation of the results. Future studies should adopt longitudinal designs to validate and expand these findings.

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Author contributions

R.A.J., C.F.P., and F.I.O. (Conception and Design), R.A.J. and C.F.P. (Acquisition of Data), F.I.O., R.A.J., and C.F.P. (Formal Analyses and Interpretation of Data), F.I.O. and R.A.J. (Drafting the Article), F.I.O., R.A.J., and C.F.P. (Revising It for Intellectual Content), F.I.O., R.A.J., and C.F.P. (Final Approval of the Completed Article).

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Conflicts of interest

C.F.P. receives royalties from Oxford University Press and is a consultant for Intiator Pharma and Pelva Health.

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