Master Thesis

Clinical Psychology

Utrecht University

Post-SSRI Sexual Dysfunction: Exploration of the Sexual Domains and Symptoms

Name: Sanjana Raj (6816983)

Supervisor: Dr. Femke van den Brink

Submission Date:

Word Count: 4353

Abstract

The aim of this study was to investigate post-SSRI sexual dysfunction (PSSD) in former antidepressant users - in comparison with a control group. In a cross-sectional design, 117 former selective serotonin reuptake inhibitors (SSRI) users (68.4% female) and 123 control participants with no history of antidepressant use (67.5% female) completed an online questionnaire assessing sexual pleasure, frequency, desire, orgasm, arousal and sexual dysfunction symptoms associated with antidepressant use. Former SSRI users reported significantly more antidepressant-associated symptoms and lower levels of sexual pleasure than the control group. Implications of these results for the understanding of PSSD in clinicians, patients and researchers are discussed. Conclusively, this study builds on the current evidence for PSSD and highlights new possibilities for research in the area.

Keywords: Post-SSRI sexual dysfunction(PSSD), selective serotonin reuptake inhibitors (SSRIs), sexual dysfunction, antidepressants

Introduction

Selective serotonin reuptake inhibitors (SSRIs) are a class of drug used widely to treat a variety of mental illnesses including depressive disorders, generalized anxiety disorders and panic disorders (Bahrick, 2008). Data from the National Health and Nutrition Examination Survey (Center for Disease Control and Prevention, 2017) in the U.S. highlighted that during 2011-2014, 12.7% of all persons aged 12 and over had taken some type of antidepressant medication in the past month. The trend towards increasing use of SSRIs over other forms of antidepressants was documented by Abbing-Karahagopian et al.'s (2014) study and is in line with the findings of previous studies (e.g. Bauer et al., 2008). Serotonin and norepinephrine reuptake inhibitors (SNRIs) work similarly to SSRIs, with the difference being that they prevent the reuptake of norepinephrine in addition to serotonin, and are often grouped together when discussing mechanisms and contraindications (Bala, Nguyen & Hellstrom, 2018; Stahl, Grady, Moret & Briley, 2005). SSRIs have been strongly implicated in symptoms of sexual dysfunction with reports ranging from 58 to 73% in users (Clayton, Croft & Handiwala, 2014). Research has documented that during treatment, SSRIs significantly affect all stages of the sexual response cycle (namely; desire, arousal and orgasm) and include symptoms such as "diminished or absent libido, arousal difficulties, erectile dysfunction, vaginal lubrication difficulties, delayed orgasm and anorgasmia" (Bala et al., 2018; Kennedy & Rizvi, 2009; Lee et al., 2010). Interestingly, SSRIs have also been marketed as treatments for premature ejaculation (Althof et al., 2014).

Post-SSRI Sexual Dysfunction

While the sexual side-effects of SSRI use are long-standing and well-documented occurrences during the course of treatment, it has been widely assumed that these symptoms would resolve after psychotropic discontinuation, albeit, with little robust evidence to back the

assumption (Bala et al., 2018; Baldwin & Foong, 2013; Healy, 2018). Literature has documented that SSRI and SNRI users experience changes in sexual functioning that persist after medication use has ceased and patients further find that their sexual functioning does not return to baseline levels, sometimes even years after the medications are no longer being used (Bala et al., 2018; Healy, 2018; Reisman, 2019). These dysfunctions have been collectively defined as post-SSRI sexual dysfunctions (PSSD) with symptoms ranging from anorgasmia, delayed orgasms, ejaculatory disturbances, diminished libido and genital anesthesia (Bolton, Sareen & Reiss, 2006; Csoka, Bahrick & Mehtonen, 2008; Kaufmann & Murdock, 2007; Reisman, 2019; Waldinger, Van Coeverden, Schweitzer & Georgiadis, 2015; Werneke & Bhugra, 2006).

Despite the emerging growth in PSSD research, there is no standard definition and conceptualization of PSSD and its symptoms (Healy, 2018). This lack of agreement within the literature stems from the challenges in identifying and defining PSSD (Healy, 2018). One such challenge is the overlap between symptoms of PSSD and depression or anxiety which offer little room for the operationalization and distinguishing of PSSD symptoms as separate from psychodynamic explanations (Reisman, 2017). These symptoms include disturbances in desire, arousal, orgasms, and psychological symptoms that affect their sexual functioning (Werneke & Bhugra, 2006). However, recent research has captured symptoms such as genital anesthesia, nipple insensitivity and orgasms without pleasure that are unique to antidepressant use and are atypical symptoms of depression and anxiety, which can aid in establishing criteria for the identification of PSSD (Ben-Sheetrit, Aizenberg, Csoka, Weizman & Hermesh, 2015; Csoka & Shipko, 2006, Healy, 2018; Healy, Noury & Mangin, 2018).

While the symptoms of PSSD are variable among patients, Csoka and Shipko (2006) outlined case reports of two men with severe penile insensitivity and loss of libido, and one

woman with high libido prior treatment that failed to return to baseline, even at much later follow-ups. The authors described further the exponential decrease in nipple sensitivity, and genital sensations that the female participant experienced within days of being on an SSRI, which when discontinued only brought back a partial return of tactile sensations. Other studies also documented evidence of post-SSRI treatment dysfunction, again with genital anesthesia and orgasms without pleasure standing out without any physical, psychological or neurobiological markers that could point to any other cause (e.g. Csoka et al., 2008, Kaufmann & Murdock, 2007). The time period between ceasing SSRI intake to continuously experiencing the severe physiological symptoms has ranged from two months to over 15 years (Ben-Sheetrit et al., 2015; Csoka & Shipko, 2006; Kaufmann & Murdock, 2007; Lareb, Netherlands Pharmacovigilance Center, 2012). A majority of these studies have been case reports with a range of 1-19 participants and very few studies have sample sizes exceeding 100 participants. The lack of sufficient research with larger groups of people and agreement upon definitions of PSSD have all made it difficult for PSSD to be recognized as an iatrogenic disorder and for clinicians to identify it, thus calling for the need for more scientific studies (Coskuner, Culha, Ozkan & Kaleagasi, 2018; Healy, 2018).

Sexual dysfunctions are on the whole associated with poorer life quality, and can have significantly adverse consequences for one's physical and mental health, interpersonal relationships and recovery from mental illness (Dennerstein, Koochaki, Barton & Graziottin, 2006; Higgins, Nash & Lynch, 2010; Marriott & Thompson, 2008; Tan, Tong & Ho, 2012; Witting et al., 2008). These dysfunctions are also significantly underreported to clinicians and can complicate the course of treatment and the collaborative alliance (Montejo, Montejo & Navarro-Cremades, 2015). The enduring complications of SSRI use are therefore particularly

vital areas of research to ensure better care for patients, more patient awareness and to aid clinicians in providing better diagnosis and care.

The Current Study

The current study aims to explore sexual dysfunction domains and symptoms reported as unique to antidepressant use in a sample of men and women that have previously taken SSRIs/SNRIs in comparison to a control group of men and women with no history of antidepressant use. Based on previous findings, it is hypothesized that former SSRI and SNRI users will have higher levels of sexual dysfunction across different domains of sexual functioning (i.e. pleasure, frequency, desire, arousal, orgasm and unique symptoms of sexual dysfunction) in comparison with the control group.

Methods

Participants and Procedure

Participants were recruited through social media sites and groups (e.g. Facebook, Instagram, Reddit). Adults (i.e. 18 years old or older) who were not using antidepressants at the time of the survey were invited to take part. This included both those who had a history of SSRI/SNRI use and people who had never used any type of antidepressants. Gorilla Experiment Builder (www.gorilla.com) was used to create and host the study. Participants accessed the questionnaire titled “Sexuality and Wellbeing” through a direct link and were able to choose whether they wished to complete the survey in English, Dutch or German. The first page of the survey had information about the purpose of the research, the criteria for participating in the study, and participants were further informed about anonymity of the data and the withdrawal procedure. Participants were only able to proceed to the study after indicating informed consent.

Following that, participants answered demographic questions (i.e. gender, nationality, age, marital status, history of antidepressant use and mental illness history). Participants were not compensated for participation and were debriefed at the end of the study. On average, the study took 25-30 minutes to complete.

An a priori analysis (G* Power) with a medium effect size (v = .06), an alpha of .05 and power .8 showed that a total sample size of 226 was sufficient to compare differences between prior SSRI users and the control group. A total of 240 participants fully completed the questionnaire. Participant ages ranged from 18 – 82 years old, with a mean age of 29.84 (SD = 10.03). A total of 67.9% of participants were women (n = 163) and 32.1% of participants were men (n = 77). Most of the participants were single (n = 147, 61.3%), and 35.4% (n = 85) of participants were married or cohabiting. The remaining 3.3% (n = 8) of participants self-reported as divorced or widowed. The participants came from 40 different countries, mostly Germany (32.1%, n = 77), India (9.6%, n = 23), United Kingdom (9.2%; n = 22), Australia (7.5%, n = 18) and the United States (7.5%, n = 18). A total of 117 (48.7%) participants had used antidepressants previously. Most of these participants (75.5%, n = 100) had used SSRIs and 14.5% (n = 17) had used SNRIS. A total of 57.3% (n = 67) of participants had not taken SSRIs in over a year and 8.7% (n = 10) had discontinued antidepressant use in the month preceding participating in the study. The remaining 34% (n = 40) had discontinued antidepressant use some time between one to twelve months prior to participating in the study. The control group consisted of 123 participants (51.2%) who reported never having used any antidepressants. An independent samples t-test showed that there were no significant differences in age between the two groups, t (237.09) = 1.96, p = .51, two-tailed. Additionally, a chi-square test showed that

there were no significant differences in the distribution of gender between the two groups, χ^2 (1, N = 240) = .02, p = .88.

Measures

All the measures were translated from English into Dutch and German by a native speaker, when a translated version was not otherwise available.

Sexual Dysfunction

The five subscales of the Changes in Sexual Functioning Questionnaire Short-Form (CSFQ-SF; Keller, McGarvey & Clayton, 2006) were used to assess levels of sexual dysfunction. The subscales assess areas of sexual functioning across the three stages (desire, arousal, orgasm) of the sexual cycle. Different versions were available for men and women to capture the aspects of sexual functioning that differ between the two (e.g. inadequate vaginal lubrication, difficulty maintaining erections). The first subscale "Pleasure" consisted of one question "compared with how enjoyable it has ever been, how enjoyable or pleasurable is your sexual life right now?" The second subscale "Frequency/Desire" was made up of two items and assessed the frequency of sexual activity and the frequency of desire experienced, e.g. "how frequently do you engage in sexual activity (sexual intercourse, masturbation, etc.) now?" The third subscale "Desire/Interest" consisted of three items that assessed levels of desire or interest in sexual activity, e.g. "how often do you become sexually aroused?" The fourth subscale "Arousal/Excitement/Erection" assessed arousal levels, e.g. "are you easily aroused?" for women or "do you get an erection easily?" for men. The fifth subscale "Orgasm/Completion/Ejaculation" assessed whether there were any dysfunctions experienced in achieving orgasms or ejaculation e.g. "how often do you experience an ejaculation?" for men and

"how often do you experience an orgasm?" for women. The Pleasure subscale was scored on a five-point Likert scale that ranged from "no enjoyment of pleasure" (5) to "great enjoyment and pleasure" (1) and the other four subscales were scored on five-point Likert scales ranging from "never" (5) to "everyday" (1). Items on the five subscales were recoded if appropriate and summed so that higher scores represent higher levels of sexual dysfunction. Both versions of the CSFQ-SF have been demonstrated to have good construct validity and internal reliability (Keller et al., 2006). In the current study, Cronbach's alpha of the four subscales that contained more than one item ranged from .79 to .88 for women, and from .65 to .80 for men.

Three additional questions were added to the study and scored separately to measure the presence and severity of dysfunctional features noted as specific to the use of antidepressants; reduced nipple sensitivity, orgasms without pleasure and genital anesthesia (Csoka & Shipko, 2006; Healy, 2018). These questions (e.g. how often do you experience numbness in your genitals?) were scored on a five-point Likert scale ranging from Never (0) to Always (4), with higher scores summed to represent more severe dysfunction. Cronbach's alpha for this scale was .74 for both women and men.

Depression

The 21-item Beck's Depression Inventory-II (BDI-II; Beck, Steer & Brown, 1996; Van der Does, 2002) was used to detect the presence and severity of depressive symptoms experienced in the two weeks prior to completing the questionnaire. The BDI-II was used in this study to control for the confounding effects of depression on sexual dysfunction symptoms. The items on the BDI-II are graded statements measuring the presence and severity of 21 different symptoms pertinent to depression such as "irritability", "sleep" and "mood". All items are scored on a four-point Likert scale which is scored from 0 (e.g. "I can sleep as well as usual") to

3 (e.g. “I wake up several hours earlier than I used to and cannot get back to sleep”). Higher total scores on the BDI-II correspond with higher levels of depression. The BDI-II is a well-established and widely used self-report measure of depression, with construct and concurrent validity (Beck et al., 1996; Van der Does, 2002). In this study, a Cronbach’s alpha of .91 was obtained for women and .92 for men.

Statistical Analyses

IBM SPSS version 25 was used to perform all statistical analyses. Means, standard deviations and bivariate correlations were calculated for all the domains of sexual functioning by former SSRI use. To test the differences in sexual dysfunction between prior SSRI users and the control group, a *Multivariate Analysis of Covariance* (MANCOVA) was used, with former antidepressant use (i.e. former SSRI/SNRI users versus the control group) as the independent variable and the domains of sexual dysfunction (i.e. sexual pleasure, frequency, desire, arousal, orgasm and the antidepressant-associated sexual dysfunction symptoms) as dependent variables. As previous research has indicated that gender is relevant when exploring sexual dysfunction (e.g. Reisman, 2019); it was included as a covariate in this analysis, along with depression to control for any confounding influence.

Results

Assumptions of normality, linearity, homogeneity of variances and multicollinearity were tested. Assumptions of normality and homogeneity of variances were violated. As group sizes were not widely different from each other and Pillai’s trace is robust to violations, the violation of homogeneity of variances were not impediments to performing the analysis (Sheehan-Holt, 1998).

Bivariate Associations, Means and Standard Deviations in Symptoms of Sexual Dysfunction

The results of the bivariate correlations, along with the means, standard deviations, maximum and minimum scores for all the dependent variables are presented in Table 1. Significant positive associations were found between all the domains of sexual dysfunction, except for the antidepressant-associated (AD) symptoms. These symptoms were only positively associated with the domains of lack of sexual pleasure and arousal.

Table 1

Means, Standard Deviations, Minimum and Maximum scores and Bivariate Correlations between the Domains of Sexual Dysfunction and Depression

Variable	Sample	*M* (SD)	Min	Max	1	2	3	4	5	6
1. Pleasure[a]	SSRI	3.39 (1.27)	1	5	-	-	-	-	-	-
	Control	2.85 (1.15)	1	5	-	-	-	-	-	-
	Total	3.11 (1.24)	1	5	-	-	-	-	-	-
2. Frequency[a]	SSRI	5.79 (1.82)	2	10	.56**	-	-	-	-	-
	Control	5.72 (1.76)	2	10	.54**	-	-	-	-	-
	Total	5.75 (1.79)	2	10	.54**	-	-	-	-	-
3. Desire[a]	SSRI	9.36 (2.80)	3	15	.49**	.68**	-	-	-	-
	Control	8.60 (2.66)	3	15	.30**	.60**	-	-	-	-
	Total	8.97 (2.75)	3	15	.42**	.63**	-	-	-	-
4. Arousal[a]	SSRI	8.37 (2.78)	3	15	.46**	.63**	.63**	-	-	-
	Control	7.82 (3.03)	3	15	.52**	.71**	.67**	-	-	-
	Total	8.09 (2.92)	3	15	.49**	.67**	.65**	-	-	-
5. Orgasm[a]	SSRI	8.02 (3.18)	3	15	.24*	.51**	.45**	.58**	-	-
	Control	7.56 (3.21)	3	15	.53**	.64**	.49**	.65**	-	-
	Total	7.78 (3.20)	3	15	.39**	.57**	.48**	.62**	-	-
6. AD Symptoms[b]	SSRI	3.21 (2.90)	0	11	.13	.08	.04	.28**	.17	-
	Control	1.78 (2.16)	0	10	.05	.04	.02	.11	-.05	-
	Total	2.48 (2.65)	0	11	.15*	.07	.07	.21**	.09	-
7. Depression[b]	SSRI	14.14(10.24)	0	46	.11	.05	.08	.17	.14	.28**
	Control	9.19 (8.15)	0	39	.27**	.29**	.17	.26**	.30**	.07
	Total	11.60 (9.54)	0	46	.23**	.16*	.15*	.22**	.22**	.26**

**p<.01; *p<.05

Sexual Dysfunction

The multivariate test for SSRI use was significant, Pillai's trace = .09, F (6, 239) = 4.11, p = .001, partial η^2 = .94 indicating large effect-size differences between former SSRI users and the control group. Gender was a significant covariate, Pillai's trace = .12, F (6, 239) = 5.48, p < .001, partial η^2 = .12, with a medium-to-large effect size. Depression was also a significant covariate, Pillai's trace = .09, F (6, 239) = 3.95, p < .001, partial η^2 =.09, with a medium effect size. This indicates that there are significant differences between former SSRI users and the control group, even when controlling for the significant variance in results that would be explained by gender and depression.

As seen in Table 2, the univariate analyses showed, that when controlling for gender and levels of depression, there were significant differences between former SSRI users and the control group with respect to the antidepressant associated symptoms of sexual dysfunction (genital anesthesia, nipple insensitivity, orgasms without pleasure), with indications of a medium effect size. Former SSRI users reported higher levels of these symptoms than the control group (Table 1). Significant differences between the groups in lack of pleasure were also found, with indications of a large effect size. Former SSRI users reported higher levels of lack of pleasure than the control group (Table 1). With respect to the other domains of sexual dysfunctions, no significant differences between the former SSRI users' group and the control group were found (Table 2).

Table 2

Univariate results for sexual dysfunction in SSRI users

DV	Predictor	*F*	df	df error	Sig	Partial η^2
SSRI	Pleasure	7.55	1	236	.006**	.03
	Frequency	.11	1	236	.746	.00
	Desire	2.64	1	236	.105	.01
	Arousal	.36	1	236	.550	.00
	Orgasm	.05	1	236	.831	.00
	AD Symptoms	11.93	1	236	.001**	.05
Gender	Pleasure	10.67	1	236	.001**	.04
	Frequency	25.97	1	236	.000**	.10
	Desire	11.20	1	236	.001**	.04
	Arousal	22.35	1	236	.000**	.90
	Orgasm	7.97	1	236	.005**	.03
	AD Symptoms	.22	1	236	.640	.00
Depression	Pleasure	7.58	1	236	.006**	.03
	Frequency	5.86	1	236	.746	.02
	Desire	3.32	1	236	.105	.01
	Arousal	10.68	1	236	.550	.04
	Orgasm	11.11	1	236	.831	.04
	AD Symptoms	9.70	1	236	.001**	.04

**$p<.01$; *$p<.05$

Discussion

The aim of this study was to investigate PSSD by comparing domains of sexual dysfunction (i.e. sexual pleasure, frequency, desire, arousal, orgasm and antidepressant-associated symptoms of sexual dysfunction) in former SSRI users, in comparison with a control group consisting of people who had never taken any antidepressants. The results indicated that the former SSRI users significantly reported higher levels of the antidepressant-associated symptoms of sexual dysfunction (i.e. genital anesthesia, nipple insensitivity and orgasms without pleasure) and less sexual pleasure than individuals with no history of antidepressant use. With respect to the other domains of sexual dysfunction (i.e. frequency, desire, arousal and orgasm), no significant differences between the former SSRI users and the control group were found.

The higher levels of antidepressant-associated symptoms of sexual dysfunction and lack of sexual pleasure in former SSRI users, suggests tentative support for PSSD. The antidepressant-associated symptoms (i.e. genital anesthesia, nipple insensitivity and orgasms without pleasure) have previously been identified as unique to the use of antidepressants and not typical symptoms of depression and anxiety (e.g., Csoka & Shipko, 2006; Reisman, 2019). Genital anesthesia in particular has been identified as the most common symptom in PSSD, often emergent at the very beginning of treatment with SSRIs (Bala et al., 2018). The lower levels of pleasure found in former SSRI users, also indicate that pleasure may be a domain of particular relevance when studying PSSD. The significant results here may be linked with the antidepressant-associated symptoms of orgasms without pleasure. The primacy of psychological symptoms in orgasms and sexual satisfaction has previously been established (e.g. Mah & Binik, 2005) and lack of pleasure may be another complex factor manifesting itself in PSSD, through

both the loss of physical sensation in orgasms and psychological enjoyment of sexual activity. Studies have found that emotional blunting or apathy is a prominent symptom in patients with sexual dysfunction during SSRI treatment (Opbroek et al., 2001; Marazziti et al., 2019; Sansone & Sansone, 2010). Opbroek et al.'s (2001) study highlighted higher levels of numbing and inabilities to experience several emotions including pleasure in people experiencing sexual dysfunction while still taking SSRIs, which they hypothesized as related to the enhancement of neurotransmitters. Emotional blunting and the difficulties in affect may therefore be a key direction through which to explore the manifestation of PSSD and may partially explain why pleasure, nipple insensitivity, genital anesthesia and orgasms without pleasure may be affected as they all relate to loss of sensation and numbing. Other explanations for this finding are put forward by Ben-Sheetrit et al. (2015) who remarked that the presence of genital anesthesia is likely to first affect decreased sexual pleasure, which can inhibit arousal and libido by negative feedback.

The results of the current study indicate support for these symptoms to be considered in the creation of validated measures of PSSD which are currently lacking in the field. These symptoms could also be useful in studies seeking to operationalize PSSD as well as to clinicians seeking to identify it in patients and monitor their treatment. The significance of symptoms such as genital anesthesia and orgasms without pleasure has implications for the professional development of clinicians since these are not typical features of sexual dysfunction, and not being able to identify them could have severe repercussions for patients and the collaborative alliance (Healy, 2018). Being educated about the potential severity and persistence of PSSD would also enable patients to make informed choices about their treatment (Bala et al., 2018; Healy, 2018). The significance of lack of pleasure, numbness and loss of sensation in genital

areas highlight possibilities for research into pleasure and loss of sensation as these could be important ways through which the disruption of sexual functioning in SSRI users can be understood. The links between previously described emotional blunting, loss of pleasure and physical sensations could provide a wider context through which the mechanisms of SSRIs can be explored (Opbroek et al., 2001, Sansone & Sansone, 2010).

The non-significant differences between former SSRI users and the control group in the domains of sexual frequency, desire, arousal and orgasm contradict earlier studies that have noted that genital anesthesia and other symptoms of sexual dysfunction correlate with lower sexual functioning across several domains and all stages of the sexual response cycle (Ben-Sheetrit et al., 2015; Reisman, 2019). These findings may suggest that the CSFQ–SF scale may not be sensitive enough to detect specific indicators of PSSD. Serreti and Chiesa (2009) also remarked that rates of sexual dysfunction vary depending on the scales used, indicating that scale sensitivity may be an essential consideration. The complexity of PSSD and the dearth of clarity regarding its mechanisms means that scales designed to measure PSSD specifically are yet to be designed. For example; it has been established that the symptoms of PSSD can manifest in a variety of ways within people with many reporting phase-specific sexual dysfunction, in the absence of global sexual dysfunction (Clayton, Keller & McGarvey, 2006; Waldinger et al., 2015).

Limitations and Directions for Future Research

Some limitations need to be acknowledged. While the current study controlled for depression using the BDI-II, other medical, sociocultural and interpersonal factors were not included, and the only strict control was that anyone on antidepressants at the time of the study could not participate. Therefore, it is unknown to what extent sexual functioning was affected by

other factors, since the variability of sexual dysfunction is greatly impacted by secondary factors (Clayton, Alkis, Parikh & Votta, 2016). Future studies should include stricter controls such as baseline levels of sexual functioning prior to SSRI treatment and aetological factors related to sexual dysfunction (other medical conditions, other medications etcetera) to rule out differential diagnosis possibilities (Werneke & Bhugra, 2006). Furthermore, differences may be prevalent even within SSRIs and SNRIs and extensive research into specific medications may assist clinicians in making more informed choices about treatments (Segraves & Balon, 2014). Sexual dysfunction has been reported with all classes of antidepressants but the nuances are yet to be captured (Taylor, Rudkin & Hawton, 2005).

There is not currently enough information on the relationship between gender and the manifestation of PSSD. Research on the whole has been contradictory on how various sexual domains are affected differently in men and women in PSSD (Clayton et al., 2006; Fooladi, Bell & Davis, 2012; Reisman, 2019; Serreti & Chiesa, 2009). Gender therefore could be an important avenue for further research in the presentation and development of PSSD. This study could also have been impacted by cultural and social factors that may have influenced participants' understanding of what levels of sexual functioning are expected and their understanding of the terms used. The participants in this study came from 40 different countries and would have likely had differences in their expectations of sexual functioning (La Torre, Giupponi, Duffy & Conca, 2013; Werneke & Bhugra, 2006). Cultural and social factors may be particularly relevant in regard to gender, with men and women's understandings and expectations of their sexuality to differ (Žourková, Češková, Hadašová, & Ravčuková). Whether or not participants were or ever had been sexually active could have also had influence over the results, as their sexual

experience and status could determine how important or noticeable any alterations in their sexual functioning were.

Conclusion

This study found that former SSRI users reported significantly higher levels of antidepressant-associated symptoms of sexual dysfunction (genital anesthesia, nipple insensitivity, orgasms without pleasure) and lack of sexual pleasure than a control group who reported no history of antidepressant use. These findings highlight that these symptoms may be particularly relevant in defining PSSD. Extensive research is required to isolate PSSD incidence from other forms of sexual dysfunction and to operationalize it accurately. PSSD is a critical issue to investigate as sexual dysfunctions can greatly impair quality of life and functioning and also complicate clinical conditions such as depression and anxiety (Kenny & Jabar, 2011; Segraves & Balon, 2014). This research has potential benefits for researchers in exploring the symptomology of PSSD as well as to empower clinicians and clients to make ethical and informed choices about treatment with SSRIs.

References

Abbing-Karahagopian, V., Huerta, C., Souverein, P. C., de Abajo, F., Leufkens, H. G. M., Slattery, J., . . . de Bruin, M. L. (2014). Antidepressant prescribing in five European countries: Application of common definitions to assess the prevalence, clinical observations, and methodological applications. *European Journal of Clinical Pharmacology,* 70, 849-857. doi: 10.1007/s00228-014-1676-z

Althof, S. E., Abdo, C. H., Dean, J., Hackett, G., Mccabe, M., Mcmahon, C. G., … Tan, H. M. (2010). International society for sexual medicines guidelines for the diagnosis and treatment of premature ejaculation. *The Journal of Sexual Medicine, 7*(9), 2947–2969. doi: 10.1111/j.1743-6109.2010.01975.x

Bahrick, A. S. (2008). Persistence of sexual dysfunction side effects after discontinuation of antidepressant medications: Emerging evidence. *The Open Psychology Journal, 1,* 42-50. doi: 10.1111/j.1743-6109.2007.00630.x

Bala, A., Nguyen, H. M. T., & Hellstrom, W. J. (2018). Post-SSRI sexual dysfunction: A literature review. Sexual Medicine Reviews, 6, 29-34. doi: 10.1016/j.sxmr.2017.07.002

Baldwin, D. S., & Foong, T. (2013). Antidepressant drugs and sexual dysfunction. *British Journal of Psychiatry*, *202*(6), 396–397. doi: 10.1192/bjp.bp.112.110650

Bauer, M., Monz, B.U., Montejo, A.L., Quail, D., Dantchev, N., Demyttenaere, K., . . . Tylee, A. (2008). Prescribing patterns of antidepressants in Europe: Results from the factors influencing depression endpoints research (FINDER) study. European Psychiatry, 23, 66-73. doi: :10.1016/j.eurpsy.2007.11.001

Beck, A. T., Steer, R. A., & Brown, G. (1996). Beck depression inventory–II. *PsycTESTS Dataset*. doi: 10.1037/t00742-000

Ben-Sheetrit, J., Aizenberg, D., Csoka, A. B., Weizman, A., & Hermesh, H. (2015). Post-SSRI sexual dysfunction: Clinical characterization and preliminary assessment of contributory factors and dose-response relationship. *Journal of Clinical Psychopharmacology, 35*(3), 273–278. doi: 10.1097/jcp.0000000000000300

Bolton, J. M., Sareen, J., & Reiss, J. P. (2006). Genital anaesthesia persisting six years after sertraline discontinuation. *Journal of Sex & Marital Therapy, 32*(4), 327–330. doi: 10.1080/00926230600666410

Center for Disease Control and Prevention. (2017). *National Health and Nutrition Examination Survey*. Retrieved from https://www.cdc.gov/nchs/nhanes/index.htm

Clayton, A. H., Alkis, A. R., Parikh, N. B., & Votta, J. G. (2016). Sexual dysfunction due to psychotropic medications. *Psychiatric Clinics of North America, 39*(3), 427–463. doi: 10.1016/j.psc.2016.04.006

Clayton, A. H., Croft, H. A., & Handiwala, L. (2014). Antidepressants and sexual dysfunction: Mechanisms and clinical implications. *Postgraduate Medicine, 126*(2), 91–99. doi: 10.3810/pgm.2014.03.2744

Clayton, A., Keller, A., & Mcgarvey, E. (2006). Burden of phase-specific sexual dysfunction with SSRIs. *Journal of Affective Disorders, 91*(1), 27–32. doi: 10.1016/j.jad.2005.12.007

Coskuner, E. R., Culha, M. G., Ozkan, B., & Kaleagasi, E. O. (2018). Post-SSRI sexual dysfunction: Preclinical to clinical. Is it fact or fiction? *Sexual Medicine Reviews, 6*(2), 217–223. doi: 10.1016/j.sxmr.2017.11.004

Csoka, A. B., Bahrick, A., & Mehtonen, O.-P. (2008). Persistent sexual dysfunction after discontinuation of selective serotonin reuptake inhibitors. *The Journal of Sexual Medicine, 5*(1), 227–233. doi: 10.1111/j.1743-6109.2007.00630.x

Csoka, A. B., & Shipko, S. (2006). Persistent sexual side effects after SSRI discontinuation. *Psychotherapy and Psychosomatics, 75*(3), 187–188. doi: 10.1159/000091777

Dennerstein, L., Koochaki, P., Barton, I., & Graziottin, A. (2006). Hypoactive sexual desire disorder in menopausal women: A survey of western European women. *The Journal of Sexual Medicine, 3*(2), 212–222. doi: 10.1111/j.1743-6109.2006.00215.x

Fooladi, E., Bell, R. J., & Davis, S. R. (2012). Management strategies in SSRI-associated sexual dysfunction in women at midlife. *Climacteric, 15*(4), 306–316. doi: 10.3109/13697137.2012.658461

Healy, D. (2018). Citizen petition: Sexual side effects of SSRIs and SNRIs. *International Journal of Risk & Safety in Medicine, 29*(3-4), 135–147. doi: 10.3233/jrs-180745

Healy, D., Noury, J. L., & Mangin, D. (2018). Enduring sexual dysfunction after treatment with antidepressants, 5α-reductase inhibitors and isotretinoin: 300 cases. *International Journal of Risk & Safety in Medicine, 29*(3-4), 125–134. doi: 10.3233/jrs-180744

Higgins, A., Nash, M., & Lynch, A.M. (2010). Antidepressant-associated sexual dysfunction: impact, effects, and treatment. *Drug, Healthcare and Patient Safety*, *2*, 141-150. doi: 10.2147/dhps.s7634

Kauffman, Robert P., and Amanda Murdock. (2007). Prolonged post-treatment genital anesthesia and sexual dysfunction following discontinuation of citalopram and the atypical antidepressant nefazodone. *The Open Womens Health Journal*,*1*(1). doi:10.2174/1874291200701010001

Keller, A., McGarvey, E. L., & Clayton, A. H. (2006). Changes in sexual functioning questionnaire--short Form. *PsycTESTS Dataset*. doi: 10.1037/t64667-000

Kennedy, S. H., & Rizvi, S. (2009). Sexual dysfunction, depression, and the impact of antidepressants. *Journal of Clinical Psychopharmacology*, *29*(2), 157–164. doi: 10.1097/jcp.0b013e31819c76e9

Kenny, M., & Jabbar, F. (2011). Sexual dysfunction and antidepressants: A review with emphasis on treatment. *Irish Journal of Psychological Medicine*, *28*(3), 165–167. doi: 10.1017/s0790966700012192

Lareb, Netherlands Pharmacovigilance Center. (2012). *SSRIs and persistent sexual dysfunction*. Retrieved from: http://databankws.lareb.nl/Downloads/KWB_2012_3_SSRI.pdf. Accessed 2017 June 1.

La Torre, A., Giupponi, G., Duffy, D., & Conca, A. (2013). Sexual dysfunction related to psychotropic drugs: A critical review - part I: Antidepressants. *Pharmacopsychiatry*, *46*(05), 191–199. doi: 10.1055/s-0033-1345205

Lee, K.-U., Lee, Y. M., Nam, J.-M., Lee, H.-K., Kweon, Y.-S., Lee, C. T., & Jun, T.-Y. (2010). Antidepressant-induced sexual dysfunction among newer antidepressants in a naturalistic setting. *Psychiatry Investigation*, *7*(1), 55. doi: 10.4306/pi.2010.7.1.55

Mah, K., & Binik, Y. M. (2005). Are orgasms in the mind or the body? Psychosocial versus physiological correlates of orgasmic pleasure and satisfaction. *Journal of Sex & Marital Therapy*, *31*(3), 187–200. doi: 10.1080/00926230590513401

Marriott, C., & Thompson, A. R. (2008). Managing threats to femininity: Personal and interpersonal experience of living with vulval pain. *Psychology & Health*, *23*(2), 243–258. doi: 10.1080/14768320601168185

Marazziti, D., Mucci, F., Tripodi, B., Carbone, M. G., Muscarella, A., Falaschi, V., & Baroni, S. (2019). Emotional blunting, cognitive impairment, bone fractures, and bleeding as possible side effects of long-term use of SSRIs. *Clinical Neuropsychiatry*, *16*(2), 75-85.

Montejo, A. L., Montejo, L., & Navarro-Cremades, F. (2015). Sexual side-effects of antidepressant and antipsychotic drugs. *Current Opinion in Psychiatry*, *28*(6), 418–423. doi: 10.1097/yco.0000000000000198

Opbroek, A., Delgado, P. L., Laukes, C., Mcgahuey, C., Katsanis, J., Moreno, F. A., & Manber, R. (2002). Emotional blunting associated with SSRI-induced sexual dysfunction. Do SSRIs inhibit emotional responses? *The International Journal of Neuropsychopharmacology*, *5*(02). doi: 10.1017/s1461145702002870

Reisman, Y. (2017). Sexual consequences of post-SSRI syndrome. *Sexual Medicine Reviews*, *5*(4), 429–433. doi: 10.1016/j.sxmr.2017.05.002

Reisman, Y. (2019). Are there any sex/gender differences in post-selective serotonin reuptake inhibitors (SSRI) sexual dysfunction (PSDD)?. *Current Sexual Health Reports*, *11*(4), 237-242.doi: 10.1007/s11930-019-00222-x

Sansone, R. A., & Sansone, L. A. (2010). SSRI-induced indifference. *Psychiatry (Edgmont)*, *7*(10).

Segraves, R. T., & Balon, R. (2014). Antidepressant-induced sexual dysfunction in men. *Pharmacology Biochemistry and Behavior*, *121*, 132–137. doi: 10.1016/j.pbb.2013.11.003

Serretti, A., & Chiesa, A. (2009). Treatment-emergent sexual dysfunction related to antidepressants: A meta-analysis. Journal of Clinical Psychopharmacology, *29*,(3), 259-266. doi: 10.1016/s0924-9338(10)70932-9

Sheehan-Holt, J. K. (1998). MANOVA simultaneous test procedures: The power and robustness of restricted multivariate contrasts. *Educational and Psychological Measurement*, *58*(6), 861–881. doi: 10.1177/0013164498058006001

Stahl, S., Grady, M., Moret, C., & Briley, M. (2005). SNRIs: The pharmacology, clinical efficacy, and tolerability in comparison with other classes of antidepressants. *CNS Spectrums*, *10*(9), 732-747. doi: 10.1017/s1092852900019726

Tan, H. M., Tong, S. F., & Ho, C. C. (2012). Mens health: Sexual dysfunction, physical, and psychological health—is there a link? *The Journal of Sexual Medicine*, *9*(3), 663–671. doi: 10.1111/j.1743-6109.2011.02582.x

Taylor, M. J., Rudkin, L., & Hawton, K. (2005). Strategies for managing antidepressant-induced sexual dysfunction: Systematic review of randomised controlled trials. *Journal of Affective Disorders*, *88*(3), 241–254. doi: 10.1016/j.jad.2005.07.006

Van der Does, A.J.W. (2002). *Manual of the Dutch Manual of the Dutch Version of the Beck Depression Inventory (BDI-II-NL).* Amsterdam: Harcourt Publishers.

Waldinger, M. D., Coevorden, R. S. V., Schweitzer, D. H., & Georgiadis, J. (2015). Penile anesthesia in post SSRI sexual dysfunction (PSSD) responds to low-power laser irradiation: A case study and hypothesis about the role of transient receptor potential (TRP) ion channels. *European Journal of Pharmacology*, *753*, 263–268. doi: 10.1016/j.ejphar.2014.11.031

Werneke, U., Northey, S., & Bhugra, D. (2006). Antidepressants and sexual dysfunction. *Acta Psychiatrica Scandinavica*, *114*(6), 384–397. doi: 10.1111/j.1600-0447.2006.00890.x

Witting, K., Santtila, P., Varjonen, M., Jern, P., Johansson, A., Pahlen, B. V. D., & Sandnabba, K. (2008). Original research—couples sexual dysfunctions: Female sexual dysfunction, sexual distress, and compatibility with partner. *The Journal of Sexual Medicine*, *5*(11), 2587–2599. doi: 10.1111/j.1743-6109.2008.00984.x

Žourková, A., Češková, E., Hadašová, E., & Ravčuková, B. (2007). Links among Paroxetine-induced sexual dysfunctions, gender, and CYP2D6 activity. *Journal of Sex & Marital Therapy*, *33*(4), 343–355. doi: 10.1080/00926230701385589