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Life after antidepressants:

Does persisting sexual dysfunction influence quality of life?

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Abstract

Selective-Serotonin Reuptake Inhibitors (SSRIs) are widely prescribed for the pharmacotherapy of mood disorders and gained much attention for their sexual side-effects. Previous research has shown that antidepressant induced sexual dysfunction may persist upon discontinuation of the therapy, which in turn negatively influences Quality of Life (QoL). As no quantitative studies with large samples are available yet, the present study aimed at establishing the prevalence of persisting sexual dysfunction as well as the relationship between sexual functioning and QoL in a sample (N = 76) of healthy adults. Results showed that 52.6% (n = 40) of participants suffered from persisting sexual dysfunction while 26.3% (n = 20) suffered from genital anesthesia and/ or nipple insensitivity. Persisting sexual dysfunction was shown to negatively influence the relationship domain of the QoL measure ($p < .001$). Participants with vs. without sexual dysfunction significantly differed in their level of relationship QoL ($F(1, 74) = 12.18$, $p = .001$, partial $\eta^2 = .141$). Therefore, clinicians need to be cautious when evaluating sexual dysfunctions and prescribing antidepressants in order to protect patients' sexual functioning and QoL.

Keywords: antidepressants, post-SSRI sexual dysfunction, persistent sexual dysfunction, QoL

Life after antidepressants: Does persisting sexual dysfunction influence quality of life?

Selective-Serotonin Reuptake Inhibitors (SSRIs) are a widely prescribed class of antidepressants and often recommended as treatment for mental disorders including major depressive disorder, obsessive-compulsive disorder, generalized anxiety disorder and social anxiety disorder (National Institute for Health and Care Excellence, 2018). Among the frequently prescribed SSRIs are fluoxetine, paroxetine, sertraline, citalopram, escitalopram, and fluvoxamine (Bahrick, 2008). Since their introduction to the market in the 1990s, SSRIs have gained wide attention regarding their side-effects, especially their profound influence on sexual functioning. Estimates conclude that 50 to 70% of patients suffer from sexual dysfunction during SSRI treatment (Montejo, Llorca, Izquierdo, & Rico-Villademoros, 2001). The most frequently cited symptoms that are experienced during treatment are diminished libido, problems with sexual arousal, delayed or muted orgasm, anorgasmia and erectile dysfunction. These symptoms in turn pose a threat to treatment compliance, as two-third of the patients discontinue their medication use due to adverse side-effects such as sexual dysfunction (Bahrick, 2008). As a consequence of rapid treatment discontinuation, the chance of relapse or developing SSRI withdrawal effects increases. Thus, it is important to investigate the impact of sexual side-effects of SSRIs and other antidepressants in order to provide better treatment decision making.

In the past years, it was generally believed and reflected in the literature that treatment emergent sexual dysfunction resolves after the cessation of the treatment and sexual functioning returns to baseline. However, in 2005 an Internet community (SSRIsex@yahoogroups.com) was founded where users reported and discussed their sexual side-effects, which in some cases did not resolve after discontinuation of the treatment. Csoka and Shipko (2006) recognized that these persistent sexual side-effects differ distinctively from the symptoms experienced during the treatment and postulated to call this post-SSRI sexual

dysfunction (PSSD). Researchers reviewed over 120 case reports and found common symptoms which seem to be characteristic of PSSD. In addition to diminished libido and sexual arousal, delayed or muted orgasm, anorgasmia and erectile dysfunction, which are common side-effects during antidepressant treatment, patients reported symptoms such as reduced genital sensation (genital anesthesia), reduced response to sexual stimuli, reduced nipple sensitivity, and decreased vaginal lubrication. The duration of the symptoms varied among patients, ranging from months up to years (Csoka & Shipko, 2008; Hogan, le Noury, Healy & Mangin, 2014).

Throughout the last decade, evidence for the existence of PSSD was established through numerous case reports (e.g., Ben-Sheetrit, Aizenberg, Csoka, Weizman & Hermesh, 2015; Ekhart & van Puijenbroek, 2014; Hogan et al., 2014) human medication studies (Safarinejad & Hosseini, 2006; Arafa & Shamloul, 2006) and animal studies (Simonsen, 2016), which confirm the persistence of sexual side-effects after SSRI treatment discontinuation. Although PSSD is not recognized as an official disorder in diagnostic manuals yet, the most recent version of the Diagnostic and Statistical Manual of Mental Disorder (DSM-5; American Psychiatric Association, 2013) describes the possibility of the persistence of SSRI-induced sexual side-effects after discontinuation of the treatment in one sentence within the chapter of Medication-Induced Sexual Dysfunction. Yet, this fact often remains unclear to many clinicians, leaving them vulnerable to unknowingly contribute to persistent sexual dysfunction (Bahrick, 2008). Thus, high-quality research, including larger samples and a quantitative approach to investigate etiological factors and the impact of these persistent effects is warranted, in order to raise awareness within the public health sector.

The extensive influence of antidepressant induced sexual side-effects becomes more pronounced when considering the following research evidence suggesting that sexual functioning has a strong impact on the Quality of Life (QoL). The World Health Organization

postulates that people's subjective perception of their QoL can be influenced by their physical health, psychological wellbeing, level of independence, personal beliefs, social relationships and their relationship to salient features of their environment (World Health Organization, 2018). By including these domains in questionnaires such as the WHOQOL-BREF, the level of QoL can be reliably assessed. Consequently, QoL may become impaired if one of the aforementioned dimensions is restricted, for example due to impaired sexual functioning. Although the few studies on the relationship between QoL and sexual dysfunction show limitations, their results can still be an indication of this relationship. For instance, Bossini et al. (2014) reported in their literature review that impaired sexual functioning may affect the sense of personal satisfaction, impair QoL and thereby negatively impact the health of the person. The inability to initiate or experience pleasure during sexual intercourse may cause unhappiness, frustration and a sense of inadequacy in sexual relationships. This in turn impacts QoL of the patient and of his or her partner and ultimately may impact relationship satisfaction. Furthermore, Naenian, Shaeriri and Hosseini (2011) compared the general health and QoL of patients with vs. without a sexual dysfunction and found that the total QoL measure was lower in patients suffering from sexual dysfunction than in the healthy control group. Stinson (2013) conducted a qualitative study about the impact of persistent sexual side-effects of SSRIs after discontinuing treatment. She concluded that the dysfunction can have substantial psychological consequences for people, both intra- and interpersonally. Specifically, subjects reported that PSSD had a negative impact on their existing relationships and further impedes the development of new relationships. These results indicate that the persistence sexual dysfunction negatively influences social and sexual lives of patients.

Although case studies and online forums have established the existence of persistent sexual dysfunction after SSRI treatment, and the reviewed studies show indications of a negative relationship between sexual dysfunction and QoL, quantitative studies with large

samples remain unavailable. As highlighted by Farnsworth and Dinsmore (2009), studies to quantify the prevalence and impact of PSSD are urgently needed, as the symptoms present more complex problems than conventional sexual dysfunctions. Therefore, the major aim of the current study was to establish the prevalence of persistent antidepressant-induced sexual side-effects and to examine the relationship between sexual functioning and QoL, using validated questionnaires in a larger sample of healthy participants (N = 76). In addition to that we aimed at establishing a first estimation of the prevalence of PSSD by including questions about common PSSD symptoms. We hypothesized that sexual functioning and QoL are moderately correlated (Hypothesis 1). More specifically, we expected that the level of QoL is determined by the presence of sexual dysfunction after SSRI treatment (Hypothesis 2). Therefore, on a group level this would imply that participants with sexual dysfunction have a lower level of QoL than participants without sexual dysfunction (Hypothesis 3). We expected that these hypotheses especially hold true for the reported quality of social relationships.

Method

Participants

An a priori power analysis (G*Power) with a medium effect size (d = 0.5), an alpha of 0.05 and a power of 0.80 indicated that a sample of 123 participants was sufficient to establish a correlation between sexual dysfunction and QoL. The current study used a total sample size of 76. Participants were recruited using both convenience and snowball sampling. Specifically, the following strategies were used to recruit participants: 1) distribution of flyers in the University and other public places (e.g., coffee shops, bars), 2) contacting (mental) health providers and requesting to lay out the flyers in their waiting area, 3) posting advertisements online on Facebook, Instagram and online forums, 4) listing the study on the Sona system website (uu.sona-systems.com). Further participants were recruited by sharing the study information with personal contacts who fit the inclusion criteria. Inclusion criteria

were age of 18 years or older, antidepressant treatment in the past and no current diagnosis of a mental disorder. Participants had the chance to win a 20€ Amazon voucher. Students who were enrolled in the Bachelor of psychology at the Utrecht University received 0.5 participation hours in return for their participation. The study was approved by the Faculty Ethics Review Board (FERB) (FETC18-099) of the faculty of social and behavioral sciences at Utrecht University, the Netherlands. All participants completed an informed consent form.

Materials and Measures

The online Gorilla Experiment Builder (www.gorilla.com) was used to create and host the questionnaire. Data were collected between 21.11.2018 and 18.03.2019. All questions were available in English, German and Dutch and participants were able to choose their preferred language. Unless otherwise stated, validated translated questionnaires were used. Social and demographic data regarding gender, age, education, origin and marital status were obtained. Furthermore, data regarding past mental health status and current and past medication use were obtained. Three additional questions regarding sexual functioning *("How often do you experience reduced genital sensation?", "How often do you experience reduced nipple sensitivity?", "How often do you experience numbness in your genitals?"*) were included to account for possible symptoms of PSSD (Csoka & Shipko, 2008; Hogan et al., 2014).

Beck's Depression Inventory. For assessing the severity of depression, Beck's Depression Inventory II (BDI-II) was included. This was necessary in order to account for possible confounding, as the presence of depression can negatively influence QoL and sexual functioning. The BDI contains 21 items, each including four alternative statements, ranked in terms of severity and scored from 0 to 3. The statements relate to common depressive symptoms, for example low mood, social withdrawal and irritability. A total score above 13 is considered as cutoff point, indicating depressive symptoms. The BDI shows high internal

consistency, high content validity, and validity in differentiating between depressed and non-depressed subjects (Richter, 1998).

Changes in Sexual Functioning Questionnaire. Sexual functioning was assessed using the clinical version of the Changes in Sexual Functioning Questionnaire for males and females (CSFQ-M-C, CSFQ-F-C). The CSFQ consists of 14 items, corresponding to categories such as sexual desire/frequency, sexual desire/interest, sexual pleasure, sexual arousal/excitement and sexual orgasm/completion. Participants respond to the items on a 5-point Likert-like scale, ranging either from *"never"* to *"every day"*, *"no enjoyment/pleasure"* to *"great enjoyment/pleasure"* or *"never"* to *"always"*. CSFQ total scores below 41 for females and below 47 for males were considered as cutoff points for indicating sexual dysfunction. The questionnaire is a reliable and valid measure of changes in sexual functioning (Clayton, Owens & McGarvey, 1995). The items show moderate to high internal consistency, the test-retest reliability is moderate to high for most of the items that were gender specific (Clayton, McGarvey & Clavet, 1997). As there are no validated German or Dutch versions of the CSFQ, we used the back-translation method to assure the best possible quality and accuracy of the translated version (Brislin, 1970).

WHOQOL-BREF. For the assessment of QoL, the World Health Organization's WHOQOL-BREF was used. The questionnaire contains a total of 26 questions, representing the domains physical health, psychological wellbeing, social relationships and environment, which are hereafter referred to as QoL domains. Sub-scores of these domains are calculated by adding up the corresponding values. No total score of QoL is available. The WHOQOL-BREF shows good internal consistency, excellent reliability and is regarded as a valid assessment of QoL in healthy participants, as well as for participants with physical or mental disorders (Skevington, Lofty & O'Connell, 2004).

Procedure

All participants who enrolled in the study had access to the same online questionnaire in either English, German or Dutch. Depending on the sex (*female/male*) of the participant, he or she received either the female or the male version of the CSFQ. Besides this distinction, all participants received the same questions with regard to content. The questionnaire was administered once per participant. No time restriction was given but filling in the questionnaire took approximately 20 minutes. After completion of the questionnaire, participants were debriefed and had the opportunity to contact the researcher or an independent complaint service in case of questions or complaints.

Analysis

All statistical analyses were performed with IBM SPSS Statistics Version 25. First, in order to establish the prevalence of sexual dysfunction in the sample, and to analyze social- and demographic data, frequency analyses and descriptive statistics were performed. To compare the group with sexual dysfunction vs. the group without sexual dysfunction, an independent- samples t-test was conducted. To test whether sexual dysfunction and QoL are moderately correlated (Hypothesis 1) bivariate associations between the included variables were explored using Pearson correlation coefficient. To test if the level of QoL is determined by the presence of sexual dysfunction after SSRI treatment (Hypothesis 2) linear multiple regression analyses using the backward method were performed. To test for interaction between sex and sexual dysfunction, an interaction term was included in the regression models. In total, four regression models were analyzed, which were each comprised of one WHOQOL-BREF domain score, (physical health, psychological wellbeing, relationship, environment) as the dependent variable and the CSFQ total score, total score for the additional questions for sexual functioning and BDI total score as independent variables. The BDI total score was included to account for possible confounding effects of depression symptoms. In order to test the hypothesis about a possible group effect of participants with sexual dysfunction vs. without sexual dysfunction (Hypothesis 3), a multivariate

analysis of variance (MANOVA) was performed, with the WHOQOL-BREF domain scores as dependent variables and presence of sexual dysfunction (yes/ no) based on the cut-off score of the CSFQ as independent variable.

Results

Social- and demographical findings

From the 76 participants (M_{age} = 29.2, *SD* = 8.76, age range 18-56), 23.7% (*n* = 18) identified as male and 76.3% (*n* = 58) as female. The majority of participants was German (86.8%, *n* = 66). A large proportion of the participants (61.8%, *n* = 47) reported being single, while 38.2% (*n* = 29) reported being in a relationship. Of all participants, the majority (53.9%, *n* = 41) reported to have a University degree. All participants took antidepressant medication in order to treat a past psychiatric illness, specifically, 6.6% (*n* = 5) suffered from Generalized Anxiety Disorder, 6.6% (*n* = 6) suffered from Post-Traumatic Stress Disorder, 77.6% (*n* = 59) suffered from Major Depressive Disorder and 9.2% (*n* = 7) suffered from a different disorder than the ones listed. Participants used antidepressant medication from 1-120 months ($M_{Medication}$ = 13.68, *SD* = 18.67) and cessation of the antidepressant treatment was due to remission of the symptoms (47.4%, *n* = 36), side-effects (43.45, *n* = 33) or a different reason (9.2%, *n* = 7). Currently, 36.8% (*n* = 28) of the participants are taking medication other than antidepressants on a regular basis, some of which are known to potentially affect sexual functioning (Conaglen & Conaglen, 2013). The mean BDI score (M_{BDI} = 15.57, SD = 10.33) in the sample exceeded the cut-off score for mild depression. An independent-samples t-test was conducted, comparing BDI mean scores of participants without sexual dysfunction vs. participants with sexual dysfunction, where it was shown that on average the groups differed in the level of depression. In essence, the group without sexual dysfunction showed no depression according to the BDI cut-off score ($M_{NO\_SexDys\_BDI}$ = 12.53, SD = 9.49), while the group with sexual dysfunction exceeded the cutoff-score for mild depression (M_{SexDys_BDI} =

18.30, SD = 10.40). This difference of -5.77, 95% CI [-10.34, -1.20], represented a medium sized effect, d = -.58), which was significant, $t(74) = -2.52$, $p = .014$. The groups did not differ significantly on the remaining variables. More information on social- and demographical findings can be found in Appendix A, Table 1.

Hypothesis 1

The prevalence of sexual dysfunction in this sample assessed by the CSFQ was 52.6% ($n = 40$). Further, 26.3% ($n = 20$) fell on the lower third of scores for the additional questions for sexual functioning, meaning that they suffered from reduced genital sensation, reduced nipple sensitivity and/ or genital numbness.

Based on the results of the correlational analyses, CSFQ scores were moderately related to the QoL relationship domain r (74) = .42, $p < .01$. Scores on the additional questions for sexual functioning were moderately related to QoL domain physical health r (74) = .32, $p < .01$, psychological wellbeing r (74) = .26, $p < .05$ and environment r (74) = .23, $p < .05$. Further correlations are reported in Appendix A, Table 2.

Hypothesis 2

In order to test the hypothesis that sexual dysfunction negatively influences QoL, multiple regression analyses were performed. All assumptions for this statistical test were met. Using the backward method, it was established that BDI score negatively predicted QoL in all four domains ($p < .001$), while CSFQ total score yielded a significant positive effect only for the relationship domain ($p < .001$), meaning that a higher CSFQ total score (i.e. higher sexual functioning) corresponded to a higher QoL. The additional questions for sexual functioning showed no significant effect. Tables 1-4 in Appendix B summarize the results.

As the inspection of the data gave the impression that the correlation between QoL sub-scores and sexual dysfunction for males were reversed, compared to females, additional correlational analyses were performed, stratified for sex. The analyses yielded indeed opposite results for males and females, implying that sexual dysfunction positively influences

QoL for males while it negatively influences QoL for females. Therefore, interaction terms were included in multiple regression analyses to test if the influence of sexual dysfunction on QoL depends on sex, however this yielded insignificant results. Thus, the analyses testing main effects were continued.

Hypothesis 3

Prior to conducting the multivariate analysis of variance (MANOVA), the assumptions for this analysis were tested and found to be met. Subsequently, a one-way MANOVA was conducted to test that there is a mean difference on WHOQOL-BREF sub-scores between participants with sexual dysfunction vs. participants without sexual dysfunction. Using Pillai's trace (Olson, 1974), a statistically significant MANOVA effect was obtained for the presence of sexual dysfunction on the WHOQOL-BREF domains, $V = .15$, $F(4, 71) = 3.21$, $p = .018$, partial $\eta^2 = .153$.

Based on the results of the Levene's Test of Equality of Error Variances the assumption was satisfied to conduct follow-up univariate ANOVAs for the QoL domains. The follow-up tests indicated that the QoL relationship domain mean score was significantly different for participants with vs. without sexual dysfunction, $F(1, 74) = 12.18$, $p = .001$, partial $\eta^2 = .141$. The comparisons with regard to the remaining QoL domains were not statistically significant.

Discussion

The focus of the present study was to establish the prevalence of sexual dysfunction after cessation of treatment with antidepressant medication and to examine the relationship between sexual functioning and QoL.

In line with previous suggestions (Montejo et al., 2001), the present study established that 52.6% of the participants suffered from sexual dysfunction (e.g. diminished libido, inadequate vaginal lubrication, erectile dysfunction, anorgasmia, painful orgasm), which was

assessed with the CSFQ. Further, 26.3% of the participants suffered from reduced genital sensation or genital numbness (genital anesthesia) and/ or reduced nipple sensitivity. This result needs to be highlighted as genital anesthesia and nipple insensitivity are found to be specific to PSSD, a disorder which is still underreported and widely unknown to clinicians, as well as to patients themselves. There are no epidemiological data available regarding PSSD yet, and thus, our result might provide a first indication of the presence of this disorder in a sample of people who previously used antidepressants. Thereby it could give a first estimation of the prevalence in the population based on a larger sample, in addition to the published case studies (Csoka & Shipko, 2008; Hogan et al., 2014). Further, it was tested if QoL can be predicted from the level of sexual functioning and if there is a difference in the level of QoL between participants with vs. without sexual dysfunction. In line with the hypotheses, it was found that sexual dysfunction negatively influences the QoL relationship domain and consequently the two groups differed in this domain. Specifically, participants suffering from sexual dysfunction showed significantly lower subjective relationship quality than their healthy counterpart. Accordingly, 14.1% of the variance in this domain is explained by the presence of sexual dysfunction. No significant results were found for the remaining QoL domains, as these seem to be independent of sexuality (e.g. satisfaction with public transport, access to public health). In fact, only the relationship domain of the WHOQOL-BREF incorporates sexual activity as factor leading to the significant findings.

Although the statistical power of the test was low due to small sample size, a high prevalence and a significant influence of sexual dysfunction on relationship quality was established. The results need to be highlighted, as sexual activity is seen as important factor for the satisfaction in romantic relationships. Research demonstrated that sexual function between partners is interdependent, meaning that sexual dysfunction in one partner can contribute to problems with sexual functioning or diminished sexual satisfaction in the other

partner (Brotto et al., 2016). Furthermore, the link between relationship satisfaction and sexual satisfaction is bidirectional (McNulty, Wenner & Fisher, 2016), consequently relationship satisfaction might be diminished if one of the partners shows impaired sexual functioning. This seems to be especially relevant if the sexual dysfunction persists for an unknown duration and no treatment is available. It is therefore important to monitor sexual functioning before, during, and after treatment with antidepressants to account for changes and intervene as soon as possible. Treatment interventions are urgently needed in order to improve sexual satisfaction and relationship quality.

Another important issue is that antidepressant induced sexual dysfunction, and specifically PSSD, is often misdiagnosed as mood disorders, which share overlapping etiologies with sexual dysfunction (Ben-Sheetrit et al., 2015). This can lead to a vicious cycle, as more antidepressants are prescribed in order to treat the supposed mood disorder. Due to these overlapping etiologies, the question was raised if the prevalence of persistent sexual dysfunction in the sample is, as hypothesized, a consequence of the antidepressant medication or rather a symptom of the mood disorder. Research has shown that depression and sexual dysfunction are difficult to disentangle, and that pleasureless orgasm was an independent predictor of depression (Ben-Sheetrit et al., 2015). In the present sample depression scores differed significantly across both groups, meaning that the group without sexual dysfunction showed no depression according to the BDI, while the group with sexual dysfunction exceeded the cutoff-score for mild depression. As the relationship between sexual dysfunction and depression can be bidirectional, it is questionable if the high prevalence sexual dysfunction is a result of the depression or if the depression developed as complication of the persistent sexual dysfunction. Symptoms such as genital anesthesia and nipple insensitivity were found to be a specific complaint after SSRI and SNRI use and did not correlate with depression or anxiety (Ben-Sheetrit et al., 2015; Bahrick, 2008). In the present sample the

majority of the participants (n = 67) used either SSRIs or SNRIs as the most recent antidepressant medication. Nevertheless, it cannot be said for certain if the presented sexual dysfunctions are a result of antidepressant use or of the mood disorder. This finding shows the importance of careful assessment of mood disorders, received pharmacological treatment and sexual functioning during the initial evaluations in order to disentangle the cause and consequence of sexual dysfunction (Brotto et al., 2016).

In general, the presence of persistent sexual dysfunction and PSSD should be considered when the symptoms reported were not present before starting antidepressant treatment, still persist after remission of the mood disorder and discontinuation of the medication and no other physical complaints can be explicable of the sexual dysfunction (Ben-Sheetrit et al., 2015). Furthermore, while mood disorders mainly influence sexual desire and arousal, antidepressant-induced sexual dysfunction includes symptoms beyond difficulties with desire and arousal, such as loss or muted orgasm and reduced sensitivity in genitals and nipples. Although it is difficult to differentiate between sexuality-related symptoms of mood disorders and persistent antidepressant induced sexual dysfunction or PSSD, the presented results show that sexual dysfunction negatively impacts relationship quality beyond depression. Specifically, by including the BDI score in the multiple regression model, it was established that the negative effect of sexual dysfunction on relationship quality significantly persists beyond depression. It is therefore crucial that clinicians know the differences between the symptoms in order to provide appropriate treatment, avoid the vicious cycle and improve QoL.

Furthermore, research established that although patients reported their mood disorder to be in remission, they still showed subthreshold to threshold symptoms (McIntyre & O'Donovan, 2004). This might explain the finding that the mean BDI score exceeded the cut-off score for mild depression in the sample. By including the BDI score in the analysis it was

found to be the best predictor of QoL, impacting all four domains negatively. Compared to sexual dysfunction, influencing the relationship domain, depression showed a broader influence on QoL. This effect of depression might result from the altered perception of oneself, the world and the future (Zimmermann, Tiellet Nunes & Fleck, 2018), which not only biases social relationships but also various other domains, such as mood, eating habits and sleep. In light of this negative and broad influence, which seems to persist beyond antidepressant treatment and despite the subjective impression to be healthy, ongoing treatment is needed in order to improve QoL. However, due to the risk of continuing the vicious cycle, clinicians should avoid prescribing more antidepressants but rather focus on the first-line treatment of mild depression, namely low-intensity psychosocial intervention or group-based Cognitive-Behavioral Therapy (CBT), thereby improving QoL as well (National Institute for Health and Care Excellence, 2018).

The presented results must be considered in light of relevant limitations. First, a sample of 76 participants was analyzed, including only 18 males, which limits the power of the tests. As the current sample was self-selected and the specific characteristics of the study population, such as origin, age and level of education might present selection bias, generalization of the results is further restricted. Furthermore, the advertisement of the study might have attracted people who were exceptionally open about their sexual dysfunction on the one hand, and deterred people with exceptionally severe sexual dysfunction on the other hand. Therefore, the prevalence estimates of persistent sexual dysfunction and PSSD should be interpreted with caution and thereby only provide a first indication of the prevalence of these problems in a sample of people who previously used antidepressant medication. Second, non-validated questions for establishing the presence of PSSD in the sample were used. Although the included questions aimed at establishing the level of genital anesthesia and nipple insensitivity, which are specific symptoms of PSSD, this is not a validated assessment

of this disorder, therefore only giving indications of possible PSSD. Third, the persistent nature of the sexual dysfunction is almost always confounded through factors such as presence of mood disorders, physical disorders or concomitant medication use. For instance, 36.8% of the participants currently use other medication, such as antihypertensives, the contraception pill, or thyroid hormones, which are known to influence sexual functioning (Conaglen & Conaglen, 2013). Moreover, the online questionnaire was cross-sectional and therefore did not establish baseline sexual functioning, which should account for the level of sexual dysfunction before antidepressant treatment was started. The retrospective nature of the CSFQ might induce recall bias, distorting the estimation of previous sexual functioning. Sexual interest and sexual orientation were not included as separate variables in the analyses. However, these are important factors, as it influences the results if participants have no interest in sexual activity or are, for instance, asexual. Future research should take these limitations into account in order to gain more reliable and valid results. Studies demonstrated that certain SSRIs and SNRIs such as sertraline, citalopram, paroxetine and venlafaxine are associated with significantly more sexual side-effects than other antidepressants, such as bupropion or vilazodone (Clayton, Croft & Handiwala, 2014). Therefore, future studies should include specific antidepressants into their analyses in order to test if the persistence of sexual dysfunction and the influence on sexual dysfunction and QoL are dependent on certain agents.

Despite the limitations, this is the first study which tried to establish the relationship between sexual functioning and QoL and give a first estimation of the prevalence of persistent sexual dysfunction and PSSD within a healthy sample of people who previously used antidepressants. Further, this study adds valuable information to the literature of antidepressant-induced sexual dysfunction, especially with regard to the underreported disorder PSSD. It was shown that persistent sexual dysfunction has widespread implications

on social relationships, which negatively influence QoL in this domain. The reported findings highlight the appeal from Brotto et al. (2016), saying that a collaboration of multidisciplinary professionals and re-evaluation of existing knowledge and application of new knowledge is needed in order to provide the best treatment of sexual dysfunction. Therefore, this thesis can be understood as an appeal to practicing clinicians on the one hand, highlighting the importance of being cautious when evaluating sexual dysfunctions and prescribing antidepressants, and as appeal to research on the other hand, as standardized diagnostic tests and treatment for PSSD are urgently needed. Clinicians need to be sensitized for PSSD and its impact, specifically, 1) that side-effects can persist upon discontinuation of antidepressant treatment, 2) how to validly assess persistent sexual dysfunction in order to decrease misdiagnoses 3) how to prevent persistent sexual dysfunction in the first place. When prescribing antidepressants, sexual functioning needs to be assessed before, during, and after treatment in order to maximize treatment effects and medication adherence. As no currently no treatment options seem to improve the symptoms of PSSD (Clayton et al., 2014), it is crucial to inform patients beforehand about potential persisting side-effects and discuss alternative medication, if needed. If (persistent) antidepressant-induced sexual dysfunction is already present, it is important that the patient receives proper psychoeducation about the disorder to end the vicious cycle of misdiagnoses and subsequent antidepressant treatment (Ben-Sheetrit et al., 2015).

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Appendix A

Social- and demographical data and bivariate correlations

Table 1

Social- and Demographic Data

	Total (*n* = 76)		With SD[a] (*n* = 40)		Without SD[b] (*n* = 36)	
	n	%	n	%	n	%
Age *mean (SD)*	29.2 (8.76)		29.03 (9.21)		29.39 (8.32)	
Gender						
Male	18	23.7	7	17.5	11	30.6
Female	58	76.3	33	82.5	25	69.4
Origin						
German	66	86.8	33	82.5	33	91.7
Other	10	13.2	7	17.5	3	8.3
Marital Status						
Single	47	61.8	23	57.5	24	66.7
Relationship	29	38.2	17	42.5	12	33.3
Education						
Higher Education	41	53.9	18	45	23	63.9
Continuing Education	17	22.4	11	27.5	6	16.7
Secondary School	16	21	9	22.5	7	19.4
Primary School	1	1.3	1	2.5	0	0
No Education	1	1.3	1	2.5	0	0
Diagnosis						
MDD	59	77.6	32	80	27	75
Social Anxiety Disorder	0	0	0	0	0	0
Generalized Anxiety Disorder	5	6.6	2	5	3	8.3
OCD	0	0	0	0	0	0
PTSD	5	6.6	1	2.5	4	11.1
Other	7	9.2	5	12.5	2	5.6

Antidepressants						
SSRIs	50	65.8	27	67.5	23	63.9
SNRIs	17	22.4	11	27.5	6	16.7
TCIs	2	2.6	0	0	2	5.6
MAOIs	1	1.3	1	2.5	0	0
Atypical Antidepressants	1	1.3	0	0	1	2.8
Other	5	6.6	1	2.5	4	11.1
Reasons Discontinuation						
Remission of Symptoms	36	47.4	18	45	18	50
Side-Effects	33	43.4	18	45	15	41.7
Other	7	9.2	4	10	3	8.3
Other Medication						
Yes	28	36.8	17	42.5	11	30.6
No	48	63.2	23	57.5	25	69.4

Note.

[a]With SD = With sexual dysfunction

[b]Without SD = Without sexual dysfunction

Table 2

Bivariate Correlations between Dependent and Independent Variables

Variables	PHYS[a]	PSYCH[b]	REL[c]	ENV[d]	Sex	BDI[e]	CSFQ[f]	Add_SD[g]
PHYS[a]	-							
PSYCH[b]	.71**	-						
REL[c]	.42**	.63**	-					
ENV[d]	.65**	.49**	.33**	-				
Sex	.06	-.13	-.18	13	-			
BDI[e]	-.71	-.69**	-.41**	-.47**	-.07	-		
CSFQ[f]	.08	.16	.42**	. 11	-.35**	-.11	-	
Add_SD[g]	-.32**	.26*	.18	23*	.03	-.33**	.15	-

*Note. *p < .05. **p < .01.*

[a] PHYS= Physical health domain WHOQOL-BREF.

[b]PSYCH = Psychological wellbeing domain WHOQOL-BREF.

[c]REL = Relationship domain WHOQOL-BREF.

[d]ENV = Environment domain WHOQOL-BREF.

[e]BDI = Beck's Depression Inventory.

[f]CSFQ = Changes in Sexual Functioning Questionnaire.

[g]Add_SD = Addition questions for sexual functioning.

Appendix B

Results of Multiple Linear Regression Analyses

Table 1

Results of Multiple Linear Regression Analysis with Physical Health as Dependent Variable

	b **[95% CI]**	**SE(b)**	**β**	**p**
Model 1				
Constant	27.07 [21.23, 32.90]	2.93		< .001
BDI[a]	-.347 [-.44, -.29]	.05	-.68	< .001
Add_SD[b]	.178 [-.15, .50]	.16	.10	.272
CSFQ[c]	-.007 [-.10, .09]	.05	-.01	.886
Model 2				
Constant	26.79 [22.39, 31.20]	2.21		< .001
BDI[a]	-.364 [-.44, -.26]	.04	-.68	< .001
Add_SD[b]	.174 [-.14, .49]	.16	.10	.273
Model 3				
Constant	29.08 [27.53, 30.63]	.78		< .001
BDI[a]	-.363 [-.45, -.28]	.04	-.71	< .001

Note. Model 1 R^2= .512. Model 2 R^2= .512. Model 3 R^2= .504.

[a] BDI = Beck's Depression Inventory.

[b] = Add_SD = Additional questions for sexual dysfunction.

[c] CSFQ = Changes in Sexual Functioning Questionnaire.

Table 2

Results of Multiple Linear Regression Analysis with Psychological Health as Dependent Variable

	b **[95% CI]**	**SE(b)**	**β**	**p**
Model 1				
Constant	19.78 [14.49, 25.06]	2.65		< .001
BDI[a]	-.301 [-.38, -.22]	.04	.67	< .001
Add_SD[b]	.049 [-.24, .34]	.15	.03	.737
CSFQ[c]	.041 [-.05, .13]	.04	.08	.352
Model 2				
Constant	20.34 [16.26, 24.43]	2.05		< .001
BDI[a]	-.305 [-.38, -.23]	.04	-.68	< .001
CSFQ[c]	.04 [-.04, .13]	.04	.08	.325
Model 3				
Constant	22.25 [20.84, 23.65]	.71		< .001
BDI[a]	-.309 [-.39, .23]	.04	-.69	< .001

Note. Model 1 R^2= .481. Model 2 R^2= .481. Model 3 R^2= .474.

[a] BDI = Beck's Depression Inventory.

[b] = Add_SD = Additional questions for sexual dysfunction.

[c] CSFQ = Changes in Sexual Functioning Questionnaire.

Table 3

R*esults of Multiple Linear Regression Analysis with Relationship as Dependent Variable*

	b *[95% CI]*	**SE(b)**	**β**	**p**
Model 1				
Constant	5.70 [1.87, 9.52]	1.92		.004
BDI[a]	-.10 [-.16, -.04]	.03	-.37	.001
Add_SD[b]	.01 [-.20, .22]	.11	.01	.943
CSFQ[c]	.12 [-.06, .18]	.03	.38	< .001
Model 2				
Constant	5.78 [16.26, 24.43]	1.48		< .001
BDI[a]	-.103 [-.38, -.23]	.03	-.37	< .001
CSFQ[c]	.12 [-.04, .13]	.03	.38	< .001

Note. Model 1 R^2= .307. Model 2 R^2= .307.

[a] BDI = Beck's Depression Inventory.

[b] = Add_SD = Additional questions for sexual dysfunction.

[c] CSFQ = Changes in Sexual Functioning Questionnaire.

Table 4

Results of Multiple Linear Regression Analysis with Environment as Dependent Variable

	b *[95% CI]*	**SE(b)**	**β**	**p**
Model 1				
Constant	28.99 [22.02, 35.96]	3.50		< .001
BDI[a]	-.22 [-.32, -.11]	.05	-.44	< .001
Add_SD[b]	.14 [-.24, .52]	.19	.08	.467
CSFQ[c]	.03 [-.09, .14]	.06	.05	.664
Model 2				
Constant	29.98 [24.71, 35.24]	2.64		< .001
BDI[a]	-.22 [-.32, -.11]	.05	-.45	< .001
Add_SD[b]	.15 [-.23, .53]	.19	.09	.430
Model 3				
Constant	31.94 [30.09, 33.79]	.93		< .001
BDI[a]	-.23 [-.33, -.13]	.05	-.47	< .001

Note. Model 1 R^2= .234. Model 2 R^2= .232. Model 3 R^2= .225.

[a] BDI = Beck's Depression Inventory.

[b] = Add_SD = Additional questions for sexual dysfunction.

[c] CSFQ = Changes in Sexual Functioning Questionnaire.