





## Sexual Medicine Reviews

Volume 10, Issue 1, January 2022, Pages 91-98

Reviews

# Post-SSRI Sexual Dysfunction (PSSD): Biological Plausibility, Symptoms, Diagnosis, and Presumed Risk Factors

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<https://doi.org/10.1016/j.sxmr.2021.07.001> 

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## ABSTRACT

### Introduction

Post-SSRI sexual-dysfunction (PSSD) is an iatrogenic syndrome, the underlying neurobiological mechanisms of which are unclear. Symptom onset follows cessation of serotonergic antidepressants i.e. Selective Serotonin and Norepinephrine Reuptake Inhibitors (SSRI's, SNRI's), and Tricyclic antidepressants (TCA's). PSSD symptoms include genital anesthesia, erectile dysfunction and orgasmic/ejaculatory anhedonia, and should be differentiated from depression-related sexual-dysfunction. Recently, accumulated data of numerous case-reports suggest additional non-sexual symptoms including, anhedonia, apathy, and blunted affect. PSSD gained official recognition after the European medical agency concluded that PSSD is a medical condition that persists after discontinuation of SSRI's and SNRI's.

## Objective

To review possible underlying neurobiological mechanisms of this syndrome, update information on the pathophysiology, present a list of potential risk-factors and discuss potential management options for PSSD.

## Methods

Extensive literature review on the main symptom-patterns of this disorder was undertaken using PubMed. It includes introductory explications of relevant neurobiology with the objective of generating hypothesis.

## Results

Precipitating factors for PSSD include previous exposure to certain drugs, genetic predisposition, psychological stress or chemical stressful reaction to antidepressants along pre-existing medical conditions affecting neuroplasticity. Different theories have been proposed to explain the pathophysiology of PSSD: epigenetic gene expression, dopamine-serotonin interactions, serotonin neurotoxicity and hormonal changes. The diagnosis of PSSD is achieved by excluding all other etiologies of sexual-dysfunction. Treatment is challenging, and many strategies have been suggested without definitive outcomes. We offer the contours of a future neurobiological research agenda, and propose several underlying mechanisms for the various symptoms of PSSD which could be the foundation for a future treatment algorithm.

## Conclusion

There is a need for well-designed neurobiological research in this domain, as well as in the prevalence, pathophysiology, and treatment of PSSD. Practitioners should be alert to the distinctive features of PSSD. Misdiagnosing this syndrome might lead to harmful treatments including reinstatement of medications which generated PSSD. Sexual Medicine Reviews.

**Peleg LC, Rabinovitch D, Lavie Y, et al. Post-SSRI Sexual Dysfunction (PSSD): Biological Plausibility, Symptoms, Diagnosis, and Presumed Risk Factors. Sex Med Rev 2022;10:91–98.**

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### INTRODUCTION

Sexual Dysfunction (SD) is often without a clear cause, but may be linked to lifestyle factors such as smoking, exposure to environmental factors (eg, heavy metals), deleterious mental states (anxiety or stress), pathological conditions (i.e. major depressive disorder, hypertension, diabetes) and medication side-effects, such as those of the widely used selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs).<sup>1</sup> ...

### METHODS

In this paper, an extensive literature review organized around the main symptomatic patterns of Post SSRI Sexual Dysfunction (PSSD) syndrome, using PubMed. Our objective is to review, as extensively as is possible, the likely neurobiological underpinnings of this disorder. It includes introductory explications of relevant neurobiology. Our overarching objective is to generate hypotheses that may become a basis for future research. Reference is also made to publicly available clinical ...

### CONCLUSION

In this manuscript, we review post-SSRI sexual dysfunction (PSSD) in terms of its biological plausibility, occurrence, symptoms, and presumed risk factors. We propose that pre-existing factors and previous drug use are implicated in triggering of PSSD and its persistent nature. Upon cessation of SSRI therapy, depressive illness may re-emerge, therefore it is of importance to note the difference between depression-related sexual dysfunction and PSSD-associated sexual dysfunction, as highlighted ...

### STATEMENT OF AUTHORSHIP

Conceptualization: L.C.P, D.B., I.G., I.H.; Data Curation: L.C.P, D.B., I.G., I.H., D.M.R.; Formal Analysis: L.C.P., I.G., Y.L., E.F., I.H.; Writing - Original Draft: D.M.R., I.G., L.C.P., E.F.; Writing - Review & Editing: D.R., I.G., L.C.P, I.H., E.F, D.M.R.; Validation: L.C.P., D.R., I.G., I.H., D.M.R. ...

## Acknowledgments

The authors wish to acknowledge Dr. David Healy for his major contribution to the research area of PSSD and Dr. Irwin Goldstein for His increased contribution to the treatment of those suffering from the syndrome. The authors would also like to acknowledge Dr. Josef Ben-Sheetrit for the important questions he raised. We acknowledge the contribution to this article by Szilard Frank. ...

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2024, Frontiers in Neuroendocrinology

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...Side effects induced by SSRI treatment generally disappear after drug discontinuation. However, in some patients, this symptomatology may also persist after stopping the drug with the occurrence of the PSSD (Bahrick, 2008; Bala et al., 2018; Csoka et al., 2008; Csoka and Shipko, 2006; Gul et al., 2023; Healy, 2019; Klaas et al., 2023; Patacchini and Cosci, 2021; Peleg et al., 2022; Reisman, 2017; Rothmore, 2020). Sexual symptoms in PSSD include decreased libido and sex drive, weak or non-pleasurable orgasm, genital anesthesia, erectile dysfunction, as well as a lack of connection between the brain and penis (Fig. 3) (Ben-Sheetrit et al., 2015; Ben-Sheetrit et al., 2023; Giatti et al., 2018b Healy et al., 2022; Laumann and Waite, 2008; Rosen et al., 1999)...

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...Additionally, the observations obtained at the withdrawal could be interesting in the context of the possible side-effects induced by paroxetine treatment. Indeed, many patients suspended the SSRI treatment for sexual dysfunction (i.e., decreased libido and sex drive, weak or non-pleasurable orgasm, genital anesthesia, erectile dysfunction, and premature ejaculation) and a small percentage of them show the persistence of this symptomatology with the appearance of the so-called post-SSRI sexual dysfunction (PSSD) (Giatti et al., 2018; Peleg et al., 2022; Healy et al., 2021; Reisman, 2020). Up to now, only sporadic self-reports on GI alterations, are present in the blog of patients (see for instance, <https://www.reddit.com/r/PSSD/> or <https://www.pssdforum.org>)...

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*Conflict of Interest:* The authors report no conflicts of interest.

*Funding:* None.

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