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PSYCHOPHARMACOLOGY OF DEPRESSION AND SEXUAL DISORDERS

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SUMMARY

Sexual dysfunctions as side effects of antidepressant treatments are being reported more and more frequently: they are one of the main reasons of dropout from therapy.

These side effects are reported in between 20% and 40% of cases.

The aim of this study is to highlight, following the actual evidence from the field of psychopharmacology, how these side effects may not be directly related to the antidepressant treatment; on the contrary we show that, following the observational clinical data obtained in our Mental Health Dept., a careful clinical interview about the sexual behaviour of the patients allows psychotherapy to interact with pharmacotherapy, in order to reduce the drug dosage, or replace it with another drug, and/or to combine an erectile dysfunction treatment with the psychopharmacological therapy.

This careful clinical interview about the sexual behavior of the patients will more clearly determine the percentages of sexual dysfunction side effects, and also avoid drop-out from antidepressant therapy.

Key words: *sexual dysfunction – depression – antidepressants – psychopharmacology - clinical interview*

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Introduction

Since SSRIs[1] and SNRIs[2] have been introduced in clinical practice it has been possible for psychiatrists to estimate their side effects as their tolerability is greater compared to tricyclics. The same can be said about other drugs such as Bupropion for the treatment of depression and anxiety problems such as panic attacks, obsessive compulsive disorder and generalized anxiety. These side effects are not lethal but they can, like sexual disorders, importantly undermine compliance with treatment (Baldwin 1995, Balon et al. 1993). Over these last 20 years, there have been many scientific publications treating different aspects of this problem: first of all, the difference between the sexual disorder caused by the medicines and that correlated with the pathology treated, then the mechanisms at the origin of such disorders and the most suitable strategies in order to face them. The most controversial problem is the prevalence of this pathology. This work is based on clinical observation of patients treated with antidepressants at our Center for Mental Health. Its first aim is to point out that the patient will talk more easily about his/her sexual disorders during a well-structured clinical interview in an empathic climate. This allows the possibility of proceeding to a therapeutic protocol which will lead, in a high percentage of cases, to good results both for the pathology and the sexual disorders. On the other hand, this work contributes to a revision of available data about the relationship between depression and sexual disorders, but also to the modalities and useful instruments which we use to measure sexual disorder and the epidemiology of the sexual disorder related to such medicines. We first discuss how the manual DSM IV[3] describes the sexual disorder resulting from medication.

Case histories in which "a clinically significant sexual disorder prevails and causes an important discomfort or interpersonal difficulties"

The anamnesis, the examination or the laboratory report points out that sexual disorder can be related in a cause and effect relationship to the use of the substances, as the symptoms appear during the taking of the substances or within the same month, or that the use of drugs is etiologically connected with the dysfunction.

Furthermore, the manual points out that: "the anomaly can neither be easily attributed to a sexual disorder not coming from the substances. In fact, the proof that the symptoms are better attributable to a sexual disorder not coming from drugs can include the following points: symptoms precede the beginning of the taking of the substances or their addiction; symptoms persist for an important period of time (about a month) after the end of the intoxication or symptoms go far beyond what we could expect in view of the type and quantity of the substances taken or the duration of the treatment. It is also possible that other data prove the existence of an independent sexual disorder not coming from the substances (for example a history of recurrent episodes not related to the taking of drugs" (APA 1994).

[1] selective medicines for the reuptake of serotonin (selective serotonin reuptake inhibitors)

[2] selective medicines for the reuptake of serotonin and noradrenalin but also others such as Bupropion (Serotonin-Norepinephrine Reuptake Inhibitors)

[3] Diagnostic and Statistical Manual - Revision 4

Furthermore, the DSM IV distinguishes 4 clinical aspects on the basis of the predominant sexual disorder:

- Impairment in desire: its predominant manifestation is insufficient or absent sexual desire;
- Impairment in excitement: its predominant manifestation is alteration in sexual excitement such as erectile or lubrication problems;
- Impairment in orgasm: its predominant manifestation is inability to perform or reach an orgasm;
- Sexual pain in which the predominant manifestation is pain associated to sexual intercourse.

These last 10 years, we have examined the scientific literature about sexual disorders available on the internet and have compared the data with those obtained from the revision of our medical records.

Studies focusing on SSRIs showed how such medicines are related, in a high percentage of cases, to sexual disorders and this percentage does not importantly vary with the different molecules. Such a percentage is quite similar for SNRIs, while many studies point out that usage of Bupropion has little effect on sexual disorders.

In the tables we can see the percentages of total sexual disorders as well as excitement and orgasm troubles associated with antidepressants. These data confirm that Bupropion is, among all drugs, the one with the lowest incidence on sexual disorder.

Table 1. Percentage of total sexual disorders, as well as troubles of desire, excitement and orgasm, associated to antidepressants

Molecules	Percentage of patients with total sexual disorder	Percentage of patients with desire troubles	Percentage of patients with excitement troubles	Percentage of patients with orgasm troubles
SSRI				
Citalopram	14-92%	40-81%	35-80%	30-53%
Escitalopram	35-48%	3%	2%	30%
Fluoxetin	14-83	8-82%	8-80%	20-52%
Fluvoxamin	11-63%	11-48%	1-21%	16-45%
Paroxetine	20-95%	16-84%	5-80%	11-63%
Sertraline	30-94%	16-83%	9-80%	13-57%
SNRI				
Duloxetine	20-46%	17%	17%	
Venlafaxine	10-93%	16-80%	20-80%	25-58%
TCA				
Clomipramine				50-92%
Imipramin	32-55%	20-27%	24-31%	24-31
OTHERS				
Bupropion	5-19%	4-6%	0-11%	0-14%
Mirtazapine	24%	20%	14%	22%

It is important to emphasize that the same studies of meta-analysis on sexual disorder related to the treatment with antidepressants by direct questions and questionnaires demonstrate an incidence of sexual disorders of 14.4% caused by the administration of placebos.

These are some of the most used scales in order to evaluate the presence of sexual disorder in patients who are treated with antidepressants:

Table 2. Most used scales in order to evaluate the presence of sexual disorder in patients treated with antidepressants

Scale	Main features	Criteria for the diagnosis of total sexual disorder
Arizona Experience Sexual Scale - ASEX	A five-item rating scale filled in by the patient. The investigated fields are: sexual desire, excitement, erection, vaginal lubrication, ability to reach orgasm and satisfaction.	>19 or any item with score 5 or 6 or 3 items with score >4
Changes in Sexual Functioning Questionnaire - CSFQ	Structured interview of 35 items (36 for men) investigating 5 fields: frequency of sexual desire (2 items), interest in sexual desire (3 items), sexual pleasure (1 item), sexual excitement (3 items) and orgasm (3 items). Further questions evaluate to what extent sexual functioning has changed in time, as well as the nature and possible causes of the changing.	<41 for women, <47 for men

The use of these scales clearly measures the incidence, type and seriousness of the sexual disorder. However, in order to give the patient the possibility to talk about this problem, it is necessary in our view to create an empathic climate that makes it easy for the patient to talk about his/her problems, as well as

involving the partner in interviews that would give the couple or the patient the possibility to tell his/her own sexual experience and possible difficulties. This would also enable the psychiatrist to give the patient helpful information in order to overcome such difficulties. We would like to emphasize the following important fact: many patients, especially women between 40 and 50 years old, say that they feel good with the ongoing therapy and that they are not interested in the limitation of sexuality even if they claim to have a sexual disorder after having taken antidepressants. In our view, this is one of the reasons why the real incidence of sexual disorder is often underdiagnosed. The psychiatrist's competence and empathy, the patient's unconditional acceptance and the consciousness that positive sexuality is an important aspect of quality of life are, according to us, the guidelines to appropriate treatment of sexual disorder. Together with psychological intervention of **a** humanistic-existential type, we can come to a joint decision with the patient on an adjustment of the pharmacological therapy. The best results were obtained with not too long half-life molecules such as Paroxetine and Sertraline, stopping taking it in the week-end, after having agreed with the patient on that we shall work together. We have also achieved good results with Bupropion, but less effective results with other methods given by literature.

In these last following two tables we can see other possible pharmacological interventions and finally the possible role of neurotransmitters.

Table 3. Possible pharmacological interventions

Intervention	Consequences	Remark
Reduction of the dosage	Resumption of the depressive symptomatology	
Treatment with Neostigmine	Myoclonus, perspiration, overflow of saliva, pollakuria, nausea, vomit, diarrhea	Valid remedy especially for problems of ejaculation (7.5-15 mg per os before sexual intercourse)
Treatment with Yohimbin (from 4 to 7.5 mg per os before sexual intercourse)	Anxiety, rise in blood pressure, irritability, trembling, pollakuria, nausea, vomit	Not on sale in Italy Valid remedy especially in case of reduction of libido or inhibition of orgasm from serotoninergic medicines
Substitution of the medicine with Bupropion	Irritability, insomnia, headache, loss of weight	
Substitution with Nefazodon	Xerostomia, nausea, headache	
Substitution with Trazodon	Risk of priapism	Valid remedy especially for erectile disorders
Substitution with Mirtazepin	Xerostomia, stypsis, sleepiness, sedation	Not enough information Valid remedy especially in case of erectile and orgasm disorders
Treatment with Ciproheptadina	Possibility to contrast the antidepressive side effect coming from the use of serotoninergic medicines	Valid remedy especially in case of orgasm disorders (4-8 mg per os, 1 or 2 hours before sexual intercourse)

Table 4. Possible role of neurotransmitters

Transmitters	Effect on animal	Effect on human being
Serotonin	Inhibition of ejaculatory response Inhibition of sexual response	Inhibition of sexual activity (clinical observations: lack of reliable experimental data)
Dopamine	Reduction in the threshold of the erectile and ejaculatory reflex Rise in sexual reaction	Improvement of the sexual reaction or no interference
Noradrenalin	- induction of the erection	Inhibition of erection Facilitation of ejaculation
Acetylcholine	- inhibition of erection following electric stimulations of the parasympathetic sacral nerves	Modulation of sexual response to the other neurotransmitters Possible facilitation of the orgasm (the microinfusion in the septal region of an epileptic woman caused continuous orgasms)

Conclusions

Sexual disorder is a considerable issue which has been underestimated until now. It can compromise conformity to pharmacological treatment. For the moment, there are no precise data about the percentage of patients who stop the pharmacological therapy because of sexual disorder emerging after the treatment with antidepressants. Such disorder should always be carefully considered, both before and after the pharmacological treatment. Different remedies have been suggested in literature but, according to us, an empathic approach of humanistic-existential type, the use of molecules such as Buproprion and a short interruption of the therapy are the choices that have given the best results in our center. All this because the pleasure of love, as Reich taught us, is the natural antagonist to anxiety from a psychological point of view. But above all because to a human being aware of death and the uselessness of traditional consolatory myths of religious and political type, love appears as the most moving expression of the complicity and existential solidarity between two human beings.

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