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Original article

## Evolution of sexual functioning of men through treated and untreated depression



### Évolution du fonctionnement sexuel des hommes durant la dépression traitée et non traitée

É.-J. Laforgue<sup>a,b,c,1,\*</sup>, G. Busnel<sup>e,1</sup>, D. Lauzeille<sup>b</sup>, M. Grall-Bronnec<sup>a,c</sup>, C. Cabelguyen<sup>a</sup>, S. Bulteau<sup>a,c</sup>, J.-M. Vanelle<sup>a</sup>, P. Jolliet<sup>b,c</sup>, A. Sauvaget<sup>a,d,\*\*</sup>, C. Victorri-Vigneau<sup>b,c,\*\*</sup>

<sup>a</sup> Addictology and Liaison-Psychiatry Department, Centre Hospitalier Universitaire de Nantes, 85, rue Saint-Jacques, 44093 Nantes, France

<sup>b</sup> Clinical Pharmacology Department, Centre Hospitalier Universitaire de Nantes, 9, quai Moncoussu, 44093 Nantes, France

<sup>c</sup> Inserm UMR 1246, Sphère, Methods in Patients-centered outcomes and Health Research, Nantes and Tours University, 22, boulevard Benoni-Goullin, 44200 Nantes, France

<sup>d</sup> (EA 4334), laboratory « Movement, Interactions, Performance », Université de Nantes, Nantes, France

<sup>e</sup> Psychiatry Department-East sector, Etablissement Psychiatrique de Loire-Atlantique Nord, Le Pont Piétain, 44130 Blain, France

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#### ABSTRACT

**Objectives.** – Depression as well as a treatment by antidepressant are factors that may interfere with sexuality. Due to this complex relationship between depression, antidepressant and sexuality, it is difficult to uncontestedly establish the exclusive accountability of a treatment or of a psychiatric disorder on sexual dysfunctions. The main purpose of the SADD (for Sexuality, Anti-Depressant and Depression) study is to evaluate sexual dysfunctions in depressed men treated with antidepressant or not.

**Methods.** – Participants of this transversal, observational study were men aged over 18 years old, suffering from unipolar major depressive disorder and treated by a psychiatrist, with or without antidepressant. Assessment of sexual functioning through three times: euthymia (before depression), untreated depression and treated depression if applicable was performed based on the ASEX scale.

**Results.** – Seventy patients were included. Eight percent of euthymic patients presented a sexual dysfunction (average score on the ASEX = 12.4) whereas 56% of untreated patients presented a sexual dysfunction (average total score on the ASEX = 17.7) and 62% (34/55) of patients treated with antidepressant (average total score on ASEX = 18.5) ( $P < 0.001$ ). Sexual functioning of men receiving treatment is not significantly different to that among men not receiving any antidepressant, even if patients treated with antidepressant reported that they had a better mood than those untreated.

**Conclusions.** – Our results reveal a high prevalence of sexual dysfunction within the framework of major depressive disorder and its treatment and underlines the complex relationship between major depressive disorder, antidepressant and sexuality.

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#### RÉSUMÉ

##### Mots clés :

Episode dépressif caractérisé

Anti-dépresseurs

Dysfonction sexuelle

Sexualité

Effets indésirables

**Objectifs.** – La dépression ainsi qu'un traitement par antidépresseur sont des facteurs pouvant interférer avec la sexualité. En raison de cette relation complexe entre dépression, antidépresseur et sexualité, il est difficile d'établir incontestablement la responsabilité exclusive d'un traitement ou d'un trouble psychiatrique sur les dysfonctions sexuelles. L'objectif principal de l'étude SADD (pour la sexualité, les antidépresseurs et la dépression) est d'évaluer les dysfonctions sexuelles chez les hommes souffrant d'un épisode dépressif majeur traités par antidépresseur ou non.

**Méthodes.** – Les participants à cette étude observationnelle transversale étaient des hommes âgés de plus de 18 ans, souffrant d'un trouble dépressif majeur unipolaire, avec ou sans antidépresseur et inclus lors

\* Corresponding author. Service d'addictologie, CHU de Nantes, 85 rue Saint-Jacques, 44093 Nantes, France.

\*\* Co-Corresponding author.

E-mail address: edouard.laforgue@chu-nantes.fr (É.-J. Laforgue).

<sup>1</sup> EJJ and GB contributed equally to the development of the manuscript and are co-first authors.

d'une consultation par un psychiatre. Les données médicales et sociodémographiques étaient recueillies lors de la consultation d'inclusion. L'évaluation du fonctionnement sexuel pendant trois différentes périodes: euthymie (avant dépression), dépression non traitée et dépression traitée le cas échéant a été réalisée sur la base de l'échelle *Arizona Sexual Experience Scale* (ASEX). L'évaluation était réalisée en un temps unique et donc rétrospective pour les périodes d'euthymie et de dépression précédant l'évaluation. L'ASEX est une échelle validée chez les hommes déprimés qui étudie de nombreux domaines du fonctionnement sexuel. L'ASEX a 5 questions relatives à différents aspects du fonctionnement sexuel : le désir, l'excitation, l'érection du pénis, l'orgasme et la satisfaction. Les autres données recueillies étaient l'évaluation de la satisfaction sexuelle par le patient selon 5 réponses possibles allant de très satisfait à très insatisfait et la thymie évaluée par le patient avec une échelle numérique de 0 (humeur la plus mauvaise possible) à 10 (euthymie). L'objectif principal était le fonctionnement sexuel dans une population d'hommes souffrant d'un trouble dépressif majeur durant trois périodes : euthymie (avant dépression), dépression non traitée et dépression traitée avec des antidépresseurs le cas échéant. Les objectifs secondaires étaient l'évaluation de la satisfaction sexuelle autodéclarée à l'égard de la vie sexuelle et de l'humeur autodéclarée. L'évolution de la fonction sexuelle a été étudiée, selon les trois périodes définies ci-dessus (euthymie, dépression traitée et dépression non traitée). Il était basé sur la comparaison des scores obtenus de l'ASEX. Dans un premier temps, nous avons utilisé le test *Silmac* afin de comparer globalement les 3 périodes. Deuxièmement, nous avons comparé les périodes 2 à 2 (*Wilcoxon* et *t-test*). Le seuil de significativité pour chaque test statistique était fixé à  $p < 0,05$ .

**Résultats.** – Soixante-dix patients ont été inclus. Huit pour cent des patients euthymiques présentaient un dysfonctionnement sexuel (score moyen à l'ASEX = 12,4) tandis que 56 % des patients non traités présentaient un dysfonctionnement sexuel (score total moyen à l'ASEX = 17,7) et 62 % des patients traités avec antidépresseur (score total moyen sur ASEX = 18,5) ( $p < 0,001$ ). Le fonctionnement sexuel des hommes sous traitement n'est pas significativement différent de celui des hommes ne recevant aucun antidépresseur, même si les patients traités par antidépresseur ont déclaré avoir une meilleure humeur que ceux non traités. Environ les trois quarts des patients ont estimé que leur vie sexuelle actuelle était une source de souffrance pour eux et 54 % ont admis être insatisfaits ou très insatisfaits. Il y avait un pourcentage significativement plus élevé ( $p < 0,05$ ) de patients avec un score  $\geq 5/10$  sur l'échelle de l'humeur d'auto-évaluation dans le groupe traité par antidépresseurs (74 %) par rapport au groupe non traité (39 %). **Conclusions.** – Nos résultats révèlent une forte prévalence de dysfonctionnement sexuel dans le cadre du trouble dépressif majeur et de son traitement et soulignent la relation complexe entre trouble dépressif majeur, antidépresseur et sexualité.

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## 1. Introduction

### 1.1. Importance and prevalence of sexual dysfunctions

Human sexuality is complex and presents multiple domains and dimensions. It is subject-dependent, influenced by numerous factors (socio-educational, cultural, religious, psychological, medical, environmental and emotional, etc.) and an integral part of good health and quality of life [1]. In this context, sexual dysfunctions (SD) are defined as “difficulties which disrupt the sexual responses of desire, vasocongestion, orgasm or any combination of these phases of sexual response” [2]. Premature ejaculation (PE) and erectile dysfunction (ED) are well described but there is limited literature on surveys addressing others SD and the global prevalence of SD. Multiple reasons are evoked: multiple study design, variations of studied populations, and always moving definitions of SD [3].

### 1.2. Relationship between depression, Antidepressants and sexual disorder

Among the factors that may interfere with sexuality, depression as well as its treatment is a key concern. It is well established that depression (e.g.: by aggravating a lack of communication within a couple, where it already exists [4] and worsening self-depreciation, guilt, shame and despair) [5–7] and the use of antidepressants (AD) are likely to interfere with sexual functioning [8,9]. There too, data are heterogeneous: prevalence of SD for patients taking AD range from 25 to 80% [10]. These differences can be explained by an under-rating of treatment-emergent sexual side effects and the different class of AD.

Despite their efficacy on depressive mood, abulia and anhedonia, AD are often accused by patients as being a source of sexual difficulties [11–13]. Serotonergic and anticholinergic action are engaged in treatment-emergent SD making tricyclic antidepressant (TCA) and selective serotonin reuptake inhibitor (SSRI) the much involved AD. Unfortunately, few patients feel free to complain about sexual difficulties spontaneously and doctors rarely dare to investigate their sexuality.

Due to this complex relationship between depression, AD and sexuality [9], it is difficult to uncontestedly establish the exclusive accountability of a treatment or of a psychiatric on SD. In this context we put in place the Sexuality, Anti-Depressant and Depression (SADD) study to evaluate SD in depressed men treated or not.

## 2. Material and method

### 2.1. Study oversight

SADD is a transversal, observational study. Participants were all enrolled by their own psychiatrist. This study was conducted with approval from the local ethics committee (*Groupe nantais d'éthique dans le domaine de la santé* notice from 20/09/16: RC 16\_0074) and in accordance with Good Clinical Practice Guidelines and the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

### 2.2. Participants

Participants were men aged over 18 years old, suffering from unipolar MDD and treated by a psychiatrist, with or without antidepressant, able to complete auto-evaluation about sexuality.

Patients with diagnosis of psychotic disorder and/or major cognitive impairment or French language disability that restrain the understanding and filling of auto-evaluation were excluded.

### 2.3. Study procedures

Participation at the study were proposed at patients by psychiatrist when they encounter inclusion criteria. If they agreed and gave oral consent to anonymous data collection, medical data (treatments, medical history) were collected by the doctor upon inclusion of the patient, then entire auto-questionnaire was handed over to the patient to be filled in. The sending back of the questionnaire was undertaken by the patient in order to guarantee the anonymity and confidentiality of the data.

A first section of the auto-questionnaire pertaining to the patient established his profile (age, sexual habits and orientation, usage of toxic substances).

A second section pertaining to the patient was presented as a table based on of the ASEX scale (Arizona Sexual Experience Scale) [14,15] over three different periods of time (euthymia before depression, untreated depression and depression treated with AD). ASEX is a validated scale in depressed men investigating many domains of sexual functioning. The ASEX has 5 questions pertaining to different aspects of sexual functioning. These are:

- desire: “how strong is your sex drive?”;
- arousal: “how easily are you sexually aroused (turned on)?”;
- penile erection “can you easily get and keep an erection?”;
- orgasm: “how easily can you reach an orgasm?” and;
- satisfaction: “are your orgasms satisfying?”.

Each item is scored from 1 to 6 with each score having a brief, simple anchor.

For example, the first item has the following anchor points for scoring:

- 1 “extremely strong”;
- 2 “very strong,”;
- 3 “somewhat strong,”;
- 4 “somewhat weak”;
- 5 “very weak”;
- 6 “no sex drive”.

The second item has the following anchor points:

- 1 “extremely easily”;
- 2 “very easily”;
- 3 “somewhat easily”;
- 4 “somewhat difficult”;
- 5 “very difficult”;
- 6 “never aroused.”

Sexual dysfunction is defined as: total 19 or more, OR 5 or more on any item, OR 4 or more on three items.

Then, sexual satisfaction was asked to be ranged by the patient according to 5 possible answers from very satisfied to very unsatisfied.

Finally, mood was self-evaluated by the patient with a numerical scale from 0 (worst mood) to 10 (euthymic mood).

### 2.4. Outcomes

The primary objective was to assess sexual functioning among a population of men suffering from a major depressive disorder (MDD) and its scalability through three times: euthymia (before

depression), untreated depression and treated depression with AD drugs if applicable. Secondary objectives were patient-reported outcomes: evaluation of self-reported satisfaction about sexual life and self-reported mood.

### 2.5. Statistical analysis

A descriptive analysis of all variables was done. The quantitative variables were expressed in the form of averages and standard deviations. The qualitative variables were expressed in the form of ratios and percentages.

The scalability of sexual function has been studied, according to the three periods of time defined above (euthymia, treated depression and untreated depression). It was based on the comparison of scores obtained from the ASEX in the second part of the questionnaire. Firstly, we used Silmack test in order to compare overall the 3 periods. Secondly, we compare periods 2 to 2 (Wilcoxon and t-test).

For each test, significance was fixed at  $P < 0.05$ . The statistical analysis was carried out on Stata11 software.

## 3. Results

### 3.1. Descriptive analysis

Seventy patients were included. Half of the patients were between 31 and 50 years old, one fifth of these were between 51 and 65 years old and approximately 10% were between 18 and 29 years old and more than 65 years old. Forty-two percent ( $n = 29/69$ ) of the patients had already been hospitalized in a psychiatric ward and 19% ( $n = 13/69$ ) had previously attempted suicide.

Concerning sexual orientation there were found to be 82.9% heterosexual, 14.3% homosexual and 3% bisexual patients. Forty-two patients (60%) were in a relationship.

At the time of recruitment, 16% ( $n = 11/69$ ) had no partner and 16% stated that they had had no sexual relations in the preceding month.

Forty-four men out of the 70 included in the study (63%) could be considered to be in currently good somatic health (i.e. no medical current issue). Previous or current medical conditions were found for 36 patients (53%): cardiovascular pathologies (16), neurological pathologies (9), endocrinological pathologies (8), carcinogenic pathologies (4), prostate pathologies (3) and pelvic trauma (1).

Half of the patients ( $n = 35$ ) were smokers with 9% smoked more than one packet per day and an average duration of smoking of 18 years. Thirteen percent of patients had an at risk consumption or chronic alcohol abuse problem and 18% stated that they took other psychoactive substances (THC, poppers, opiates, cocaine, amphetamines).

Twenty-two patients (31%) declared that they had received no help for the sexual difficulties they had encountered. At the opposite, 27% ( $n = 19/70$ ) had consulted a doctor or a sexologist, 13% ( $n = 9/70$ ) had benefitted from a medicine designed to help with sexual difficulties. Some patients ( $n = 8/70$ ; 11%) had resorted to the use of toxic substances (alcohol, drugs).

At the time of recruitment, 57 patients (81.4%) received at least one line of AD treatment, among which 77% were SSRI or serotonin noradrenaline reuptake inhibitor (SNRI). Five patients (8.7%) were receiving a combination of 2 AD.

The treatment duration was less than one year for 72.2% ( $n = 39/54$ ) of these patients.

The most prescribed molecules were: venlafaxine (24.6%), escitalopram (17.5%), fluoxetine (15.8%), mirtazapine (10.5%).

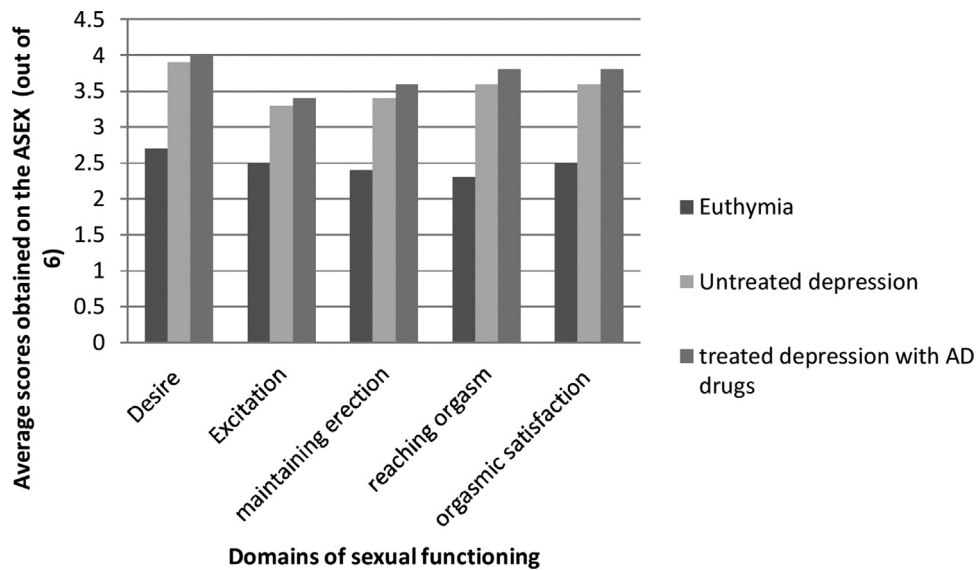


Fig. 1. Average scores obtained on the ASEX according to the presence or not of a mood disorder and AD treatment.

### 3.2. Primary outcome

According to the ASEX criteria, 8% (5/63) of euthymic patients presented a SD (average score on the ASEX = 12.4) whereas 56% (33/59) of untreated MDD patients presented a SD (average total score on the ASEX = 17.7) and 62% (34/55) of MDD patients treated with AD drugs (average total score on ASEX = 18.5). The sexual functioning of euthymic patients is shown to be significantly ( $P < 0.001$ ) less impacted in the domains explored by the ASEX than that of patients suffering from MDD, whether treated or not by AD. On the other hand, using the same criteria, sexual functioning of men with MDD receiving treatment is not significantly different to that among men with a MDD not receiving any AD treatment. Fig. 1 represents the average scores obtained on the ASEX by patients for each sexual domain.

### 3.3. Secondary outcomes

About three quarters of patients ( $n = 51/69$ ) estimated that their current sexual life was a source of suffering for them and 54% ( $n = 38/70$ ) admitted to being either dissatisfied or highly dissatisfied (Fig. 2).

There was a significantly ( $P < 0.05$ ) higher percentage of patient with a score of  $\geq 5/10$  on auto-evaluation mood scale in the treated with AD group 42/57 (74%) versus untreated group 5/13 (39%).

## 4. Discussion

### 4.1. Main results

Our results reveal a very high prevalence of SD within the framework of MDD and its treatment, which made it almost systematic. All the phases of sexual response are impacted and all types of SD are observed among MDD patients with a higher prevalence than that of the general population [16]. These findings are compatible with previous studies [11,17,18], in particular with the study entitled ELIXIR [19]. This highlights the consistency of our approach.

Problems of desire seem to be the most troublesome and unsatisfactory amongst men suffering from MDD. These patients probably experience heightened negativity as they attribute their state as being at the source of their sexual difficulties.

If three quarters of patients declared themselves to be suffering sexually and 69% were totally dissatisfied with their sexuality, only 27% consulted a doctor and only 13% declared that they had benefited from medication (IPDE5). In the ELIXIR study, only 35% of patients suffering from MDD spontaneously spoke to their doctor about their SD [19]. This paradox can be linked to the discomfort or even the shame felt by some patients when discussing SD with a doctor, above all if the latter does not seem to be receptive to or understanding of this type of difficulty.

### 4.2. Sexual dysfunctions assessment

International classifications such as the DSM-5 [10] and ICD-10 [20] recognize and define a decrease in sexual desire, erectile problems, PE and delayed ejaculation (DE) as sexual dysfunctions [21,22]. However, certain dysfunctions, although not specifically described in these classifications, are important to investigate such as aspermia (or dry ejaculations), anejaculation, sexual anhedonia and anorgasmia [5,11,17,19,23]. Different tools can be used to screen and follow up SD [24]. In this regard, there are many questionnaires which evaluate sexuality. After studying several sexological tools, Lukacs considered it important to investigate 7 domains (desire, sexual life, sexual relations, erection, penetration, orgasm and ejaculation) with, for each domain, three dimensions: functional, discomfort and satisfaction [25]. He applied this method to 8 validated questionnaires. He highlighted their inequality in the exploration of sexuality and estimated that they provide a heterogeneous and incomplete perception. We used the ASEX scale for its simplicity in our exploratory study. But our results emphasize the importance of broadly evaluating all areas of sexuality.

### 4.3. Sexuality, depression and antidepressant

With respect to moods, patients treated with AD drugs stated that they had a better morale than those untreated using patient reported outcomes. Mood disorders are significantly improved when treated with AD drugs. Nevertheless, patients suffering from a MDD who receive AD drug treatment have significantly highest ASEX score, as the non-treatment patients, than euthymic patients. And beyond the significant difference, it is interesting to note that euthymic patients have an average ASEX score on all items less than 3. Each ASEX item is rated from 1 to 6, with 6 being the highest pejo-

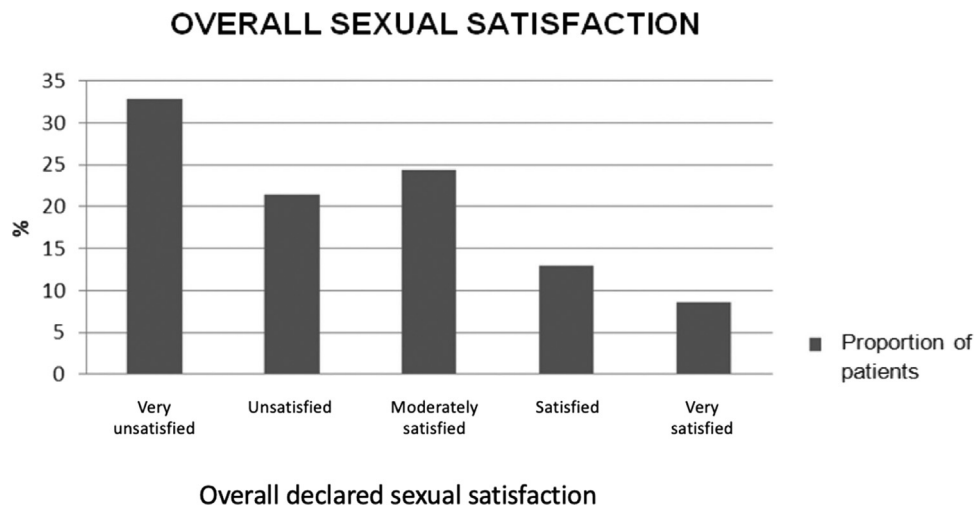


Fig. 2. Spread of patients according to their overall declared sexual satisfaction.

rative score. The interest of a 6-item rating is that when you do not exceed three, you are in the “easily” or “strong” category depending on the items. When we exceed 3, we go into the category “difficult” or “weak” depending on the items. Conversely, depressive patients treated or not have a score on all ASEX items well above 3.

Although the SADD study does not show a significant difference of sexual functioning between patients suffering from MDD that are treated and those that are untreated (probably due to a lack of statistical strength of the study), we did note slightly higher average scores on the ASEX among patients receiving treatment. However, this difference is too minimal to have any significant clinical credibility. One cannot conclude that untreated patients have higher SD rates in comparison with treated patients. Thus, remission from MDD does not seem to be sufficient to restore a satisfactory sexuality. Two hypotheses can explain this: under these conditions one cannot exclude the possibility that AD drugs directly disturb sexual function, or during antidepressant administration, it can be hypothesized that thymia is improved before sexual disorders.

It is difficult to formally establish the accountability of psychiatric disorders or treatment side effects. In fact, most of the time SD have multiple etiologies and over and above the psychiatric, anatomical and pharmacological dimensions; one must take into account educational, societal, emotional, conjugal and chronological factors [26]. Sexual functioning is possibly, due to its complexity, the last symptom to disappear during remission from MDD.

#### 4.4. SD characteristics

Concerning the SD found within the framework of MDD, some thought must be given to the following. Problems with sexual desire are more frequent among MDD patients regardless of their socio-affective status. Erectile dysfunction is equally very largely represented, amongst treated patients as well as amongst patients not receiving any AD treatment. This ED is probably linked to anxiety, responsible for an ortho-sympathetic reaction, which is incompatible with the erectile reflex [9,27].

One must however note that half of the patients were smokers since, on average, the age of 18. Smoking is a risk factor for cardiovascular diseases and an atheromatous agent, which can induce erectile problems in certain patients [26].

The differences of prevalence concerning certain SD in the SADD study in comparison with other studies, can be explained by the fact that 91% of patients were recruited in the psychiatric unit. These patients were more likely to suffer from a severe or resistant form of

MDD, with stronger AD drug treatments in comparison to patients followed in general medicine.

#### 4.5. Strengths and limitations

One of the strengths of the SADD study was the exploration of the sexual satisfaction of patients and of the disruption in their sexual life during depression. We limited the loss of information by asking doctors to inform the medical and surgical antecedents, as well as treatment and toxics used. This information allowed us to nuance the results and not to impute the sexual difficulties noted entirely to MDD.

This study has also the merit of having studied SD from a minimum amount of data judged to be useful and pertinent from a Sexology point of view which allow the evaluation of sexual functions in the most reliable, exhaustive and direct way.

The ASEX is a validated and commonly use tool of screening of SD and evaluation of sexual functioning that made our main objective robust. Furthermore, it is validated in French [15]. Collecting data about two or three different period for the patient can be subject to bias of evaluation, memorization, etc. and dependent on response shift. Multiple and differed evaluation for patients with mood disorder about their sexuality expose to a major risk of losing patients. Also, this prospective method does not guarantee the absence of memorization bias and response shift. In regard of these arguments we made the choice of a unique evaluation with retrospective collection in order to simplify the assessment and maximize the data collection.

We deliberately choose self-reported evaluation for the secondary objectives. This choice stands mainly on the important subjective part of both sexuality and mood disorders. Also, for mood disorder as MDD the importance of functional outcomes treatment have already been reported in the literature [28]. Furthermore patient-reported evaluation have shown to be as effective as clinician rating scales (as MADRS, HAM-D) for MDD [29].

Despite these arguments, our study has some limitations. First, the number of patients (n=70) is too low to split population in subcategory and it is possible that some results were not significant due to this parameter. This is particularly obvious for comparison of SD in elderly vs. non-elderly patients (our study is limited in this respect as our sample includes only 10% of men over the age of 65 years), treated vs. untreated patient and different class of antidepressant. It was not possible to determine if the SD were more frequent with certain classes of AD drug. Notably, it is well known that mirtazapine shows different sexual dysfunction

rate in comparison versus serotonergic ones. In the same vein, health issues, medication by other psychotropic as antipsychotic or somatic treatment as beta blocker and intake of IPDE-5 can be confounders bias.

#### 4.6. Perspectives

If SD are a real consequence of AD, one must underline that untreated patients suffering from MDD seem to suffer as much from SD as those who are treated. Sexual disorders are present from the onset of depression; it is therefore not desirable to wait until patients complain about SD, or until AD treatment is prescribed to investigate sexuality. This is especially true, as it has been formally established that the alleviation of sexual disorders contributes to the improvement of moods through the restauration of feelings of self-worth and self-confidence [9,23,28]. Moreover, AD have a classical delay of 2–3 weeks to the onset of efficacy, that is progressive through time with a possibility that sexual functions recovery can take some weeks more. Likewise, this element can contribute to a retarded self-evaluation of mood improvement.

Given the impact of SD on treatment adherence, following the scalability of sexual satisfaction during a treatment by AD is a key point. Based on this, a dialogue between the clinician and the patient must be set up. Correlation between SD scalability and MDD relief is to address, thereby the risk of AD drop-out due to sexual side effects attributed by the medication will maybe improve.

It does not seem necessary to characterize SD in clinical research. The usage of a simple and concise tool such as the ASEX is pertinent for evaluating the scalability of sexual functioning, among patients suffering from MDD, in the main domains: desire, excitation, orgasm, and satisfaction. Nevertheless, the characterization of SD is useful in clinical practice as a basis to propose therapeutic strategies and by default to orientate patients towards a specialist in sexuality (sexologist, urologist, and gynecologist) in order to favor a good quality of life and to limit the risk of inobservance.

#### 5. Conclusion

Although the study presents limits, SADD strove to characterize and establish the prevalence of all observable SD within the framework of MDD and its treatment. This study enhances current knowledge of this syndrome while providing a focus on overall sexual satisfaction and discomfort felt by patients with respect to their sexuality during MDD.

SADD is in coherence with previous studies and therefore underlines the close and complex relationships that exist between psychiatric illness, AD drug treatment and sexuality. The harmful role of AD drugs on sexual functioning cannot be ignored and additional studies in this field are required.

Nevertheless, it seems that sexual disorders are frequent during MDD before any medical treatment is initiated. Their screening and treatment are therefore an essential part of patient care and allow for the improvement of quality of life, a good doctor-patient relationship and greater therapeutic adherence.

We therefore feel that the connection of psychiatric care with sexology is an issue of paramount importance.

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#### Disclosure of interest

The authors declare that they have no competing interest.

#### Author contributions

GB, DL, PJ, AS, CVV: conceived of or designed study.  
EJL, GB, CC, SB: performed research.  
EJL, GB, DL, CVV: analyzed data.  
MGB, JMV, AS: contributed new methods or models.  
EJL, GB, DL, CVV: wrote the paper.

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