

Emotional blunting following long-term antidepressant treatment

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Introduction

In the last decades, the use of antidepressants, particularly of selective serotonin reuptake inhibitors (SSRIs) has increased progressively, so that nowadays they represent one of the most commonly prescribed drugs in the medical practice (Bauer et al., 2008; Pratt et al., 2011). This is due to different factors, such as their indication and significant effectiveness in both depression and anxiety disorders, coupled with fewer side effects and lower toxicity/lethality, as compared with older antidepressants (Stahl, 2008). Currently, the wide use of SSRIs has been also promoted by the easier recognition and prompter psychiatric diagnoses, as well as acceptance of psychotropic medications by patients and clinicians (Borch-Jacobson, 2002; Paulose-Ram et al., 2007; Olsson and Marcus, 2009). Undoubtedly, if on one side SSRIs are very effective in improving some negative and debilitating symptoms of depression, on the other, they seem to dampen some rewarding and joyful emotions (Barnhardt et al., 2004). Therefore, nowadays a greater concern is emerging that SSRIs may provoke previously unrecognized side effects, such as cognitive and/or emotional blunting and apathy. In the scientific literature, such effects have been also named SSRIs-induced indifference, but disagreements exist on how to label this phenomenon (Wongpakaran et al., 2007; Price et al., 2009). Some reports are available showing that patients treated for long periods with SSRIs experience decreased emotional response to both aversive and pleasurable events. Taken together, such data would indicate that SSRIs would blunt positive emotions and potentially alter personality (Kramer, 1993; Opbroek et al., 2002; Sansone and Sansone, 2010). Although depressed patients may suffer from anhedonia even after clinical remission (Raskin et al., 2012), emotional blunting seems to be a different phenomenon strictly related to SSRI intake (Price and Goodwin, 2009).

At the moment, as there are no large epidemiological studies on this topic, data on the prevalence rate of SSRIs-induced emotional blunting should be interpreted with caution.

Given the paucity of information on this topic and the total absence of data in our country, the aim of this paper was to explore and compare the eventual changes of some components of loving relationship during a long term-treatment of depression with SSRIs and tricyclics (TCAs). For this purpose, we developed a specific instrument, the so-called “Sex, Attachment, Love” Questionnaire (SALT) (Appendix 1: translation into English of the original questionnaire in Italian). The possible differences between men and women were examined as well.

Materials and methods

Subjects

The study sample included 192 outpatients (123 women and 69 men, mean age±SD: 41.2±10.2 years) who were recruited amongst a large cohort of patients suffering from mood disorders at the outpatient unit of the Dipartimento di Medicina Clinica e Sperimentale, Section of Psychiatry, at Pisa University. They were selected on the basis of a primary diagnosis of major depression, according to DSM-IV-TR (American Psychiatric Association, 2000) criteria, and assessed by the Structured Clinical Interview for DSM-IV (SCID, First et al., 2002) and the Hamilton Rating Scale for Depression (HRSD, Hamilton, 1960). All subjects had to be treated with one antidepressant only, either SSRI or TCA, for at least six months, to suffer from mild or moderate depression, as shown by their HRSD total scores, and they had to be involved in a loving relationship. Nineteen patients were affected also by panic disorder, 16 by obsessive-compulsive disorder and one by social phobia. None suffered from a major physical illness or took other medications besides antidepressants. Only twenty-one (11 women and 10 men) patients referred that they had used sporadically benzodiazepines or antihistamine compounds for sleep problems or panic attacks.

The most used SSRI was paroxetine (n. 26), followed by escitalopram (n. 24), citalopram (n. 20), sertraline (n. 17), fluoxetine (n. 15) and fluvoxamine (n. 7). Clomipramine (n. 35) was the most prescribed TCA followed by imipramine (20), amitriptyline (n. 12), trimipramine (9) and nortriptyline (8).

Fifty-eight patients had completed 13 years of school, 45 had a University degree and the remaining had completed between 10 and 8 years of school.

Most of the patients were office and governative workers (75), 42 were business managers, 35 were manual workers and 20 were traders. The rest of the sample included 15 housewives, 3 university students, and 2 unemployed.

A large majority of the subjects was married (n. 117, 60%), 47 (24%) was living with the partner, and the remaining 29 (15%) was living alone.

Instrument

The Sex-Attachment-Love Test (SALT) is a 40 items self-report questionnaire aimed at exploring the possible variations of three dimensions typical of loving relationships, that is to say, sex, attachment and love.

The SALT is scored on a three points likert scale, where 3 (answer “a”) represents “less than before”, 2 (answer “b”) “as before”, and 1 (answer “c”) “more than before”. “Before” is to be intended as “before the beginning of the psychopharmacological treatment”.

The instrument was developed by organizing “a priori” the forty items in three groups, each corresponding to a specific dimension: “Sex” (items # 25-40), “Attachment” (items # 2-8; # 17-20; # 24), “Love” (items # 1; # 9-16; # 21-23), each conceptualized as follows, on the basis of the literature suggestions.

1) To build the items of the “Sex” dimension, we referred to the DSM-IV-TR (APA, 2000) criteria of sexual disorders, for men and for women. These items explore the desire for physical contact with the partner, at both behavioral (strategies to reach proximity and facilitate and/or reach contacts) and ideative (sexual fantasies) levels, as well as frequency and quality/satisfaction of sexual intercourses. One probe question (item # 35) determines whether a specific situations is applicable to the patient. If the answer to the probe question is 3 and the participant is a man, the question 40 should be answered.

2) The items of the “Attachment” dimension were built according to the Bowlby's attachment theory (Bowlby, 1969, 1973, 1980; Hazan and Shaver, 1987; Brennan et al., 1998; Marazziti et al., 2007). The partner is considered as an attachment figure when the four characteristics differentiating an attachment relationship from all other are present: seeking closeness, separation anxiety, secure base, and safe haven (Ainsworth, 1989).

3) The Sternberg's triangular theory of love (1986) was chosen to build up the “Love” dimension. According to Sternberg, when love is present the partner is seen as a separate person, preferred over others, with intimacy, passion and devotion being typical emotional aspects.

The SALT proved to be acceptable and required 15 minutes on average to be completed.

One hundred seventy-nine subjects were heterosexual and 13 homosexual. All referred that they were involved in a loving relationship (length: between 7 and 316 months, mean±SD: 150±136 months) prior to the beginning of the psychopharmacological treatment (duration: between 6 and 107 months, mean±SD: 23±25).

The study was approved by the Ethics Committee of the University of Pisa and all subjects gave their informed written consent to participation.

Statistical Analyses

SALT questionnaires were considered valid if they contained less than 10% missing items. Comparison of parametric data were carried out with ANOVA, and that of percentage of answers with chi-square analysis. Three two-way factorial ANOVA analyses were used to study the effect of gender and drug, included the possible interaction between them, on each dimension. As the interaction was significant, we continued the analysis within the therapeutic groups.

All statistical procedures were conducted using SPSS, version 12.0.1.

Results

All patients included in the study returned the SALT questionnaires that were correctly fulfilled and therefore could be processed.

Seventy-six women and 33 men were taking one SSRI, while 48 women and 36 men one TCA. No inter- or intragroup significant differences were detected in terms of length of the psychopharmacological treatment, or of loving relationship, as well as of type of work and education. The mean drug doses and the mean HRSD total scores were similar in all groups and subgroups.

The two-way ANOVA analysis of variance (factorial model) showed that there was a significant interaction effect of drug X gender on two domains, in particular “Love” (F(1,182)=4.41, p=.037) and “Sex” (F(1,185)=7.56, p=.007). This means that effect of drug is different in the two sexes. In fact, the total score of the “Love” domain was higher in men taking SSRIs (25.71±5.35 vs 23.18±6.99, t=2.13, p=.036), and that of the “Sex” domain in women taking TCAs (32.06±6.03 vs 35.70±6.99, t=-2.41, p=.019) (table 1).

After analyzing and comparing the single items between patients taking SSRIs or TCAs (and with answers “less than before” vs “more than before plus as before”), some significant differences were observed. The patients taking SSRIs showed higher percentages of answers “less than before” than those taking TCAs at the following items: # 2 “I feel at ease in sharing with my partner thoughts and feelings” (24.2% vs 11.6%, chi square=4.45, p=.035), # 3 “I address my partner for advice or help” (24.2% vs 10.1%, chi square=5.65, p=.017), # 4 “I address my partner for support and reassurance” (24.2% vs 8.7%, chi square=7.02, p=.008), # 5 “I consider my partner a referral for my uncertainties” (27.4% vs 10.1%, chi square=7.91, p=.005), # 6 “I rely on my partner easily” (29.8% vs 8.7%, chi square=11.45, p=.001), # 7 “The perspective of losing my partner frighten me” (19.4% vs 8.7%, chi square=3.84, p=.050), # 13 “I wish the love I feel for my partner lasts forever” (20.2% vs 8.7%, chi square=4.323, p=.038) (table 2).

When the patients were divided in men and women, some significant differences could be recorded (in this case, for a reliable analysis, the item # 40 was excluded because it pertained to men only). The men taking SSRIs had a higher percentage of answers of type a (“less than before) on the item # 3 (“I address my partner for advice or help”, 37.5% vs 15.8%, chi-square=7.56, p=.006), and # 11 (“I take care of my partner”, 39.7% vs 16.7, chi-square=4.27, p=.001) than women. The women taking TCAs had a higher percentage of answers “less than before” in the majority of items related to the sexual life and performances # 25 (“I am sexually attracted by my partner”, 42.4% vs 19.4%, chi-square=4.29, p=.038); # 26 (“I seek for sexual intimacy with my partner”, 57.6% vs 27.8%, chi-square=6.28, p=.012); # 29 (“I have sexual fantasies about my partner”, 45.5% vs 16.7%, chi-square=6.74, p=.009); # 30 (“I often recall the moments of passion with my partner”, 36.4% vs 13.9%, chi-square=4.68, p=.030); # 31 (“The proximity to my partner sexually arouse me”, 57.6% vs 33.3%, chi-square=4.09, p=.043); # 33 (“I take the initiative for sex”, 60.6% vs 25.0%, chi-square=8.96, p=.003); # 36 (“The number of orgasm is..”, 69.7% vs 36.1%, chi-square=7.78, p=.005); # 38 (“If I think to be unfaithful to my partner, this happens..”, 30.3% vs 11.1%, chi-square=3.92, p=.048) (table 3).

Some additional analyses were carried out after dividing the patients with short and long duration of the relationship, while setting the limit less/more than 12 months, respectively. The ensuing findings showed that there was a higher percentage of answers “less than before” at the item # 4 (“I address my partner for support and reassurance”) in patients with a shorter (< 12 months) vs a longer relationship (26.2% vs 11.2%, chi square=2.34, p=.002) and taking SSRIs vs those taking TCAs (35.7% vs 7.1%, chi square=2.54, p=.001). The same was true for the item # 5 (I consider my partner a referral for my uncertainties, 26.7% vs 8.8%, chi square=2.52, p=.001), and # 8 (I need confirmations from my partner, 29.3% vs 7.0%, chi square=3.13, p=.001) (data not shown).

Discussion

Currently, an increasing attention is being directed towards the emergence of emotional side effects, the so-called “emotional blunting” or “apathy” or “indifference”, following the use of SSRI antidepressants (Barnhardt et al., 2004; Wongpakaran et al., 2007; Price et al., 2009). However, no systematic study has been carried out to explore the real prevalence of this phenomenon. In addition, the majority of data was gathered in small samples of patients that are not easily comparable being adults, children, out- or inpatients, recruited in different settings (Murphy et al., 2000; Bollin and Kohlenberg, 2004; Fava et al., 2006; Opbroek et al., 2002; Sato and Asada, 2012; Reinblatt and Riddle, 2006; Garland and Baerg, 2001). Further, even the assessment of the different features was rather heterogeneous, and the instruments explored different emotional domains, traits or symptoms, whose definition was often arbitrary with poor construct validity (Opbroek et al., 2002; Price et al., 2009; Sansone and Sansone, 2010).

Therefore, we planned the present study to explore and compare specific problems that might have emerged in a loving relationship after the long-term use of SSRIs or TCAs, through a new questionnaire called “SALT” investigating the main component of a loving relationship, that is to say, sex, attachment and love (Bowlby 1969, 1973, 1980; Sternberg, 1986; Hazan and Shaver, 1987; Ainsworth, 1989; APA, 2000). In addition, the recruitment of the patients was carried out according to strict inclusion criteria: they had to be outpatients suffering from mild-to moderate depression in partial or full remission, as shown by the HDRS total score (between 5 and 15), to take one antidepressant only for at least six months, and to be involved in a loving relationship. More important, all patients were adults of both sexes, within a limited age range, as emotions can be impaired in elderly people (Sullivan and Ruffman, 2004). Although women were preponderant in our sample (123 vs 69), this is not surprising given the prevalence of the female sex in depression and taken into account the naturalistic recruitment for this study (Hirschfeld, 2012).

The results showed that 109 patients taking SSRIs and 84 TCAs. No inter- or intragroup differences in the length of the pharmacological treatment or loving relationship, mean drug doses and HRSD total scores, were detected.

The main finding was that the interaction between drug and sex produced a significant effect on “Love” and “Sex” domains. In fact, the total score of the first was higher in men taking SSRIs, while that of “Sex” in women taking TCAs. These findings would indicate that SSRIs provoke more impairment of the love feelings in men taking SSRIs, while women show more disturbances of the sexual life if taking TCAs. According to our knowledge, these findings represent the first observations of a dimorphic effect of SSRIs and TCAs in the two sexes.

Specifically, SSRIs seem to provoke more alterations of some emotional features than TCAs, but only in men, while women seem to be “preserved” by this side effect, because perhaps their emotions are different and deeper than in men (Fisher et al., 2006; Marazziti et al., 2010a; 2010b).

In addition, after the analyses and comparisons of percentage of answers to single items between patients taking SSRIs and TCAs, or in men and women taking the two classes of antidepressants, other significant data did emerge. First, there was a significant impact of the SSRIs on items of both “Love” (# 1, # 13) and “Attachment” (# 2, # 3, # 4, # 5, # 6, # 7) dimensions. In general the patients felt less committed to and detached from the partner than before the beginning of the treatment, partner that, in turn, appears less reliable. The possibility of losing his/her partner is less frightening than before and the wish that the love may last for ever is attenuated. Second, the impairment of the attachment feelings was particularly evident in men taking SSRIs. Interestingly, in spite of the reported decreased libido, men taking SSRIs continued to pursue sexual intimacy and to complete satisfactory sexual intercourses. This is at variance with the reported and patented sexual side effects of SSRIs, but this might be due to our small sample size, or cultural reasons for refusal to admitting physically sexual problems typical of mediterranean men (Cimbalo and Novel, 1993; Bozon and Kontula 1998; Rizzi, 2004; Colson et al., 2006). However, we cannot exclude that there might be a positive effect of antidepressants in sexual performances in men, given the evidence of the high prevalence (between 50% and 75%) of such symptoms in untreated depressed patients (Kennedy et al., 1999). Women taking both SSRIs and TCAs did not report significant impairment of the love and attachment feelings, while those taking TCAs showed a significant alterations of their sexual life, as documented by the answers at the items # 25, # 26, # 29, # 30, # 31, # 33, # 36, and # 38. Therefore, women taking TCAs seem to suffer more from sexual side effects than men, with no impairment of the feelings towards the partner, because love is more important than sex to women (Cimbalo and Novell, 1993; Fischer et al., 2006).

Moreover, the duration of the relationship seems to offer a sort of “protection” against the onset of some side effects during antidepressant treatment. In fact, some items related to the “attachment” dimension were more common in patients taking SSRIs of both sexes, but with a short (< 12 months) relationship length.

The main bias of the present study is that the size of the group of patients taking SSRIs or TCAs was not similar, but this reflects the clinical reality and the prevalent use of SSRIs over TCAs nowadays (Rosholm et al., 2001; Lockhart and Guthrie, 2007; Bauer et al., 2008). Second, the small sample size did not permit the analysis of the effect of single compounds, that have a quite heterogenous spectrum of pharmacological activity (Stahl, 2008), as well as of the different doses of each drug. Similarly, for the same reason, we could not compare patients with different comorbid disorders. Third, although it is well known that personality factors are associated with sexual dysfunctions (Eysenck, 1971, 1972; Costa et al., 1992), we did not include a personality assessment. Fourth, the SALT questionnaire was not yet validated.

In spite of the decreasing use of TCAs worldwide for the treatment of depression in favour of SSRIs, as these last show a more tolerable side effect profile, our findings support the notion that they provoke remarkable emotional side effects. Perhaps a forum should be promoted in order to reconsider their most appropriate use and to what extend they should replace TCAs (Rosholm et al., 2001). In addition, the different sensitivity of the two sexes to emotional or sexual side effects, provoked by SSRIs and TCA, strongly suggests that future studies assessing the side effects of antidepressants should take into account the gender variable.

Table 1

Comparison of the score of the three SALT domains (A=Attachment, L=Love, S=Sex) in men and women taking SSRIs and TCAs.

SSRIs		
	M	W
S	34.81 ± 5.91	32.46 ± 8.48
A	26.08 ± 5.61	24.12 ± 6.72
L	25.71 ± 5.35	23.18 ± 6.99*

TCAs		
S	32.06 ± 6.03	35.70 ± 6.52**
A	23.58 ± 5.22	24.30 ± 4.86
L	23.29 ± 5.69	24.72 ± 5.34

* Significant, t=2.13, p=.036)

** Significant, t=-2.41, p=.019).

Table 2

Comparison of percentage of single items between patients taking SSRIs or TCAs and wi answers “less than before” vs “more than before + as before” (only significant data are reported)

# 2 “I feel at ease in sharing with my partner thoughts and feelings”		
SSRIs: 24.2%	TCAs: 11.6%	(chi square=4.45, p=.035)
# 3 “I address my partner for advice or help”		
SSRIs: 24.2%	TCAs: 10.1%	(chi square=5.65, p=.017)
# 4 “I address my partner for support and reassurance”		
SSRIs: 24.2%	TCAs: 8.7%,	(chi square=7.02, p=.008)
# 5 “I consider my partner a referral for my uncertainties”		
SSRIs: 27.4%	TCAs: 10.1%	(chi square=7.91, p=.005)
# 6 “I rely on my partner easily”		
SSRIs: 29.8%	TCAs: 8.7%	(chi square=11.45, p=.001)
# 7 “The perspective of losing my partner frighten me”		
SSRIs: 19.4%	TCAs: 8.7%	(chi square=3.84, p=.050)
# 13 “I wish the love I feel for my partner lasts forever”		
SSRIs: 20.2%	TCAs 8.7%	(chi square=4.323, p=.038)

Table 3

Comparison of percentage of single items between men and women taking SSRIs or TCAs (only significant data are reported)

SSRIs		
	M	W
# 3 “I address my partner for advice or help” (chi-square=7.56, p=.006)	37.5%	15.8%,
# 11 “I take care of my partner” chi-square=4.27, p=.001)	39.7%	16.7
TCAs		
# 25 “I am sexually attracted by my partner” (chi-square=4.29, p=.038);	42.4%	19.4,
# 26 “I seek for sexual intimacy with my partner” (chi-square=6.28, p=.012)	57.6%	27.8%
# 29 “I have sexual fantasies about my partner” (chi-square=6.74, p=.009;	45.5%	16.7%
# 30 “I often recall the moments of passion with my partner” (chi-square=4.68, p=.030)	36.4%	13.9%
# 31 “The proximity to my partner arouses me” (chi-square=4.09, p=.043)	57.6%	33.3%
# 33 “I take the initiative for sex” (chi-square=8.96, p=.003)	60.6%	25.0%
# 36 “The number of orgasm is.. (chi-square=7.78, p=.005)	69.7%	36.1%
# 38 (“If I think to be unfaithful to my partner, this happens..” chi-square=3.92, p=.048)	30.3%	11.1%

Emotional blunting following long-term antidepressant treatment

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Purpose of the study: Given the paucity of information on this topic and the total absence of data in our country, the aim of the present study was to explore and compare the eventual changes of some components of loving relationship during a long term-treatment of depression both selective serotonin reuptake inhibitors (SSRIs) and tricyclics (TCAs). For this purpose, we developed a specific instrument, the so-called 'Sex, Attachment, Love' Questionnaire (SALT). The possible differences between men and women were examined as well.

Methods: The sample was composed by 192 outpatients (123 women and 69 men, mean±SD age: 41.2±10.2 years), suffering from mild or moderate depression, according to DSM-IV-TR criteria, who were selected if they were treated with one antidepressant only for at least six months and were involved in a loving relationship.

The Sex-Attachment-Love Test (SALT) is a 40-item self-report questionnaire aimed at exploring the possible variations of three dimensions typical of romantic relationship, that is to say, sex, attachment and love. The SALT was developed by organizing 'a priori' the forty items in three groups, each corresponding to a specific dimension: 'Sex' (items #25-40), 'Attachment' (items #2-8; #17-20; #24), 'Love' (items #1; #9-16; #21-23).

Results: The two-way ANOVA analysis of variance (factorial model) showed that there was a significant interaction effect of drug × gender on two domains, in particular 'Love' [F(1,182)=4.41, p=0.037] and 'Sex' [F(1,185)=7.56, p=0.007]. This means that effect of drug is different in the two sexes. In fact, the total score of the 'Love' domain was higher in men taking SSRIs (25.71±5.35 vs 23.18±6.99, t=2.13, p=0.036), and that of the 'Sex' domain in women taking TCA (32.06±6.03 vs 35.70±6.99, t=-2.41, p=0.019).

The results showed that SSRIs had a significant impact on the feelings of love and attachment towards the partner especially in men, while women taking TCAs complained of more sexual side effects than men. These data were supported also by the detection of a significant interaction between drug and sex on the 'Love' and 'Sex' domains.

Conclusions: The main finding of our study was that the interaction between drug and sex produced a significant effect on 'Love' and 'Sex' domains. In fact, the total score of the first was higher in men taking SSRIs, while that of 'Sex' in women taking TCAs. These findings would indicate that SSRIs provoke more impairment of the love feelings in men taking SSRIs, while women show more disturbances of the sexual life if taking TCAs. According to our knowledge, these findings represent the first observations of a dimorphic effect of SSRIs and TCAs in the two sexes. Specifically, SSRIs seem to provoke more alterations of some emotional features than TCAs, but only in men, while women seem to be 'preserved' by this side effect, because perhaps their emotions are different and deeper than in men.

The present findings, while demonstrating a dimorphic effect of antidepressants on some component of loving relationships, need to be deepened in future studies.

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