Changes in dream experience in relation with antidepressant escitalopram treatment in depressed female patients: a preliminary study

Studio sulla variazione dell'esperienza soggettiva del sogno in pazienti depressi in corso di trattamento antidepressivo

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RIASSUNTO. Introduzione. Sleep disturbances have long been considered as a cardinal symptom of endogenous depression and dreams in depressed patients usually differ from those of healthy people. The aim of the present study was to investigate dream subjective experiences and their modifications in relation to clinical response in a group of escitalopram-treated depressed patients. **Methods.** Twenty-seven female patients meeting DSM-IV-TR criteria for Major Depressive Disorder (MDD) and starting SSRI therapy were included in the study. Data about psychopathological status and dreaming subjective experiences were collected at baseline (T0), 4 weeks after the beginning of the treatment (T1) and after further 4 weeks of therapy (T2). **Results.** At T0 dream experience was impaired and negatively toned. Concomitantly with the decrease of symptoms severity, the 8-week escitalopram treatment yielded to significant improvements in the recall of both quantity and quality of dreams; those patients whit lower clinical benefits kept on reporting impaired dream experiences. **Discussion.** The results of the present study evidence how the changes in some specific dreaming characteristics, such as the subjective recall of dream activity, the dream recall quality, the dream emotional content and the dream complexity represent reliable markers of the effectiveness of antidepressant therapy.

KEY WORDS: depression, dream, sleep disturbances, psychopharmacology, escitalopram.

RIASSUNTO. Introduzione. Le anomalie del sonno REM nei pazienti depressi sono state ampiamente studiate e documentate. L'effetto del trattamento farmacologico antidepressivo si traduce nella riduzione di questa fase del sonno. L'esperienza dell'attività onirica nei pazienti depressi varia nel corso della terapia antidepressiva. **Metodi.** Sono stati inclusi nello studio 40 pazienti affetti da disturbo depressivo che necessitavano di trattamento farmacologico. Attraverso la somministrazione di questionari, ideati per l'analisi dell'esperienza soggettiva del sogno, sono state esplorate le seguenti variabili: quantità del sonno, quantità dei sogni, percezione del momento della notte di maggiore attività onirica, colorito emotivo dei sogni, qualità del ricordo dei sogni e loro complessità. Tali variabili sono state messe in relazione all'andamento della sintomatologia depressiva, valutata attraverso la Montgomery-Asberg Depression Rating Scale (MADRS). La MADRS e i questionari sono stati somministrati nel corso della prima visita (T0), e dopo 4 e 8 settimane di trattamento farmacologico (rispettivamente T1 e T2). **Risultati.** Parallelamente alla durata del trattamento antidepressivo, i pazienti hanno riportato un aumento della propria attività onirica (T0-T2: p=0,001), una variazione in senso positivo del colorito emotivo (T0-T1: p=0,003; T0-T2: p<0,001), un ricordo più chiaro (T0-T2: p=0,001) e una riduzione della complessità dei sogni (T0-T2: p=0,008). **Conclusioni.** Esistono variazioni dell'esperienza soggettiva del sogno nel corso del trattamento farmacologico antidepressivo. I pazienti riferiscono un aumento dell'attività onirica, un colorito emotivo meno negativo, un ricordo del sogno più chiaro, una minore complessità dei contenuti. Sebbene nel corso del trattamento un maggior numero di pazienti riferisca un momento di maggiore attività onirica prima del risveglio, tale dato non è risultato essere statisticamente significativo.

PAROLE CHIAVE: fase REM, attività onirica, disturbo depressivo, disturbi del sonno, psicofarmacologia, escitalopram.

INTRODUCTION

Sleep disturbances have long been considered as a cardinal symptom of endogenous depression. Objectively, polysomnographic studies of depressed patients evidenced that the internal sleep organization is impaired with reduced latency of the first REM sleep episode associated to increased density of REM sleep, a percentage reduction of the total length of deep Slow Wave Sleep (SWS) and an increase in night awakenings[1-3].

Consistently with the abnormalities of sleep organization, dreams in patients with depression usually differ from those of healthy people. During depression, dreams have been reported to be shorter and less frequently remembered[10]. Their temporal perspective is generally restricted, with a preponderance of elements pertaining to the past; the setting is usually known and the dream characters are mostly family members[11-14].

Common depressive themes, such as loss, death, separation have been showed to be prevalent in a number of studies[15,16]; in addition, some authors reported a high frequency of dreams with unpleasant contents, labelled "masochistic", in which the dreamer was the recipient of rejection, disappointment, humiliation, or similar unpleasant experiences[6,7,17,18].

Several studies showed that antidepressant pharmacological treatments were associated with increased dream recall frequency[5,19-22] and with positive changes in dream emotional content[12-18]. However, contradictory data are present on the topic: some studies reported a decrease of dream recall frequency under tricyclic antidepressants[21,22], phenelzine[20], and SSRIs[20] and unchanged or increased negative dream emotions in patients completely recovered from their depressive episodes[5,23].

In this context, the aim of the present study was to investigate dream subjective experiences and their modifications in relation to clinical response in a group of escitalopram-treated depressed patients. Among the antidepressant drugs, escitalopram was chosen as it is the most selective SSRI[24]. To minimize variability due to gender differences, only female subjects have been included in the study.

METHODS

Twenty-seven female patients meeting DSM-IV TR criteria for Major Depressive Disorder (MDD) and starting SSRI therapy were included in the study. Patients were recruited at the outpatient psychiatric clinic of the A. Fiorini University Hospital, Sapienza University of Rome. All participants gave written informed consent and underwent an extended clinical interview by a fully certified consultant psychiatrist.

Subjects with any of the following were excluded: history of psychiatric disorders other than MDD or neurological disorders; lifetime substance abuse; antidepressant pharmacological treatment before the beginning of the study or concomitant use of additional medications.

Clinical data of patients were collected at baseline (T0), 4 weeks after the beginning of the treatment (T1) and after further 4 weeks of therapy (T2).

MDD severity was assessed using the Montgomery-Asberg Depression Rating Scale (MADRS) and the Beck Depression Inventory (BDI). The dream experiences were assessed through two specific questionnaires: the Subjective Experience of Dream questionnaire 1 (SED 1) at T0, that investigated the dream experience in the 4 weeks before T0, and the Subjective Experience of Dream questionnaire 2 (SED 2) at T1 and T2, that investigated the changes in dream experience between T0, T1, and T2. The two questionnaires have been specifically designed by our research team[25] to explore the following dream parameters: subjective recall of dream activity (increased, unchanged, decreased); period of the night with recall of maximum dream activity (throughout the night, just after falling asleep, before awakening), recall of dream quality (clear, confused); dream emotional content (positive, neutral/variable, negative), and dream complexity (increased, unchanged, decreased).

Statistical analyses

Statistical analysis was performed using SPSS V16 (SPSS Inc., Chicago, IL, USA). Crosstabs and χ^2 test were carried out to assess changes over the course of treatment in the different dream parameters. Repeated-Measures ANCOVAs with time as within-participant factor and age as covariate were carried out to assess clinical changes (MADRS and BDI total score). MANCOVA, yet covarying for age, was finally used to compare MADRS and BDI total scores according to the different patients' dream characteristics (Bonferroni correction applied). The significant threshold was set at $p \leq .05$.

RESULTS

Over the course of treatment, $\chi 2$ test revealed a significant enhance in the number of patients reporting an increased subjective dream activity [T0-T2, $\chi^2(1)=12.79$, $p<.001$; T1-T2, $\chi^2(1)=5.08$, $p=.024$], a clear dream recall quality [T0-T2, $\chi 2(1)=6.13$, $p=.013$], a positive dream emotional content [T0-T2 and T1-T2, $\chi 2(1)=4.42$, $p=.036$], and a reduced dream complexity [T0-T2, $\chi^2(1)=5.59$, $p=.018$]. A significant enhance was also found in the number of patients reporting as period of sleep with maximum dream activity the one just before awakening [T0-T2, $\chi 2(1)=6.31$, $p=.012$] (Table 1). Over the course of treatment, repeated-measures ANCOVAs showed a significant improvement in both the MADRS and BDI scores [MADRS, F (2,50)=6.87, $p=.002$; BDI (*Greenhouse-Geisser* correction), F (2,50)=5.74, $p=.012$]. At T2, MANCOVA revealed a significant effect of dreaming on both the MADRS and BDI scores [subjective dream activity, *Pillai's Trace, F* (4,46)=4.56, $p=.003$; dream emotional content, *Pillai's Trace*, F (4,46)=4.99, $p=.002$; and dream complexity, *Pillai's Trace*, $F(4,46)=3.95$, $p=.008$]. Separate univariate ANCOVAs specifically revealed higher MADRS and BDI scores in patients kept on reporting a decreased subjective dream activity [MADRS, $F(2,23)=9.82$, $p=.001$; *post-hoc* pairwise comparisons: MADRS decreased-increased, 21.75±9.74 vs 8.14±4.80, $p=.001$; MADRS decreased-unchanged, 21.75±9.74 vs 6.89±5.77, $p=.001$. BDI, $F(2,23)=11.13$, $p<.0001$, *post-hoc* pairwise comparisons: BDI decreased-increased, 20.25±7.89 vs 6.86±3.86, $p<.0001$; BDI decreased-unchanged, 20.25±7.89 vs 7.78±6.16, $p=.001$], a negative dream emotional content [MADRS, $F(2,23)=16.36$, $p<.0001$, *post-hoc* pairwise comparisons: MADRS negative-positive, 29.50±3.53 vs 8.00±5.34, $p<.0001$; MADRS negative-neutral/variable, 29.50±3.53 vs 8.23±5.48, $p<.0001$. BDI, $F(2,23)=11.15$, $p<.0001$, *post-hoc* pairwise comparisons: BDI negative-positive, 26.00±7.07 vs 7.37±3.56, $p=.001$; BDI negative-neutral/variable, 26.00±7.07 vs 8.00±5.66, $p<.0001$], and an increased dream complexity [MADRS, $F(2,23)=9.35$, $p=.001$; *post-hoc* pairwise comparisons: MADRS increased-decreased, 20.67±10.26 vs 5.55±5.32,

Table 1. Crosstabs and Fisher or $\chi 2$ test results of the comparisons amongst T0,T1, and T2 of the different dream characteristics within patients with MDD (Major Depressive Disorder)

	T0 MDD (*n*=27)	T1 MDD (*n*=27)	T2 MDD (*n*=27)	*p*
Subjective recall of dream activity				
Increased	2	6	14	T0-T2=.001; T1-T2=.024
Unchanged	8	15	9	n.s.
Decreased	17	6	4	T0-T2<.001
Period of the night with recall of maximum dream activity				
Throughout the night	12	10	6	n.s.
Just after falling asleep	3	2	0	n.s.
Before awakenings	12	15	21	T0-T2=.012
Recall of dream quality				
Clear	11	15	20	T0-T2=.013
Confused	16	12	7	T0-T2=.013
Dream emotional content				
Positive	2	2	8	T0-T2; T1-T2=.036
Neutral/variable	13	4	2	T0-T1=.008; T0-T2=.001
Negative	12	21	17	T0-T1=.012
Dream complexity				
Increased	14	7	3	T0-T2=.001
Unchanged	11	14	15	n.s.
Decreased	2	6	9	T0-T2=.018

p=.001; MADRS increased-unchanged, 20.67±10.26 vs 10.07±6.45, *p*=.008. BDI, $F(2,23)=4.17$, *p*=.028; *post-hoc* pairwise comparisons: BDI increased-decreased, 17.00±12.49 vs 7.55±5.96, *p*=.028; BDI increased-unchanged, 17.00±12.49 vs 8.53±5.72, *p*=.042] (Table 2). No significant differences were found in the MADRS and BDI scores according to the remaining patients' dream characteristics (Table 2).

Table 2. MANCOVA results of the comparisons at T0,T1, and T2 of the MADRS and BDI total scores according to the different patients' dream characteristics (Bonferroni correction applied)

	T0 MADRS/BDI	T1 MADRS/BDI	T2 MADRS/BDI
Subjective recall of dream activity			
Increased	26,50±0.71/ 40.00±5.66	22.83±6.24/ 13.33±4.27	8.14±4.80/ 6.86±3.86
Unchanged	31.75±6.67/ 26.50±8.81	18.80±10.97/ 17.67±6.54	6.89±5.77/ 7.78±6.16
Decreased	31.82±7.83/ 26.41±6.63	17.33±9.02/ 16.67±4.41	21.75±9.74/ 20.25±7.89
P	n.s/n.s.	n.s/n.s.	MADRS *De-In* and *De-Un* =.001/ BDI *De-In*<.001 and *De-Un* =.001
Period of the night with recall of maximum dream activity			
Throughout the night	32.25±6.74/ 26.00±8.41	20.10±10.65/ 18.70±6.60	10.67±11.38/ 10.00±11.21
Just after falling asleep	37.00±6.56/ 27.00±7.81	27.00±7.07/ 15.00±11.31	-
Before awakenings	29.17±7.36/ 29.00±7.78	17.87±9.11/ 15.20±4.39	9.48±6.64/ 8.90±5.63
P	n.s./n.s.	n.s./n.s.	n.s./n.s.
Recall of dream quality			
Clear	32.45±7.42/ 26.73±9.24	18.60±9.70/ 15.07±5.19	10.70±8.12/ 9.30±7.77
Confused	30.69±7.18/ 27.94±7.10	20.33±9.77/ 18.25±6.21	7.00±5.94/ 8.71±4.46
P	n.s./n.s.	n.s./n.s.	n.s./n.s.
Dream emotional content			
Positive	31.50±6.36/ 34.00±2.83	22.00±0.00/ 20.00±4.24	8.00±5.34/ 7.37±3.56
Neutral/variable	27.75±6.00/ 28.33±6.58	21.05±9.24/ 16.43±6.33	8.23±5.48/ 8.00±5.66
Negative	34.77±7.07/ 25.61±9.11	9.25±8.14/ 15.00±2.31	29.50±3.53/ 26.00±7.07
P	n.s./n.s.	n.s./n.s.	MADRS *Neg-Pos* and *Neg-Neu*=.001/ BDI *Neg-Pos*=.001 and *Neg-Neu*<.001
Dream complexity			
Increased	32.42±6.13/26. 33±7.04	25.71±6.10/ 15.14±5.18	20.67±10.26/ 17.00±12.49
Unchanged	31.00±8.54/ 29.61±8.57	19.86±9.29/ 18.78±5.41	10.07±6.45/ 8.53±5.72
Decreased	28.00±4.24/ 20.00±2.83	10.83±8.01/ 12.67±5.54	5.55±5.32/ 7.55±5.96
P	n.s./n.s.	MADRS *In-Dec*=.020/ n.s	MADRS *In-De*=.001 and *In-Un*=.008/ BDI *In-De*=.028 and *In-Un*=.042

DISCUSSION

Biorhythm distrurbances are common in depression as well as in other psychiatirc disorders[26-28]. The results of the present study seem to confirm earlier findings of an impaired dream experience in patients with depression.

For what concerns the dreaming assessment at T0, the difficulty in remembering dreams, already found in patients with depression in many previous studies[5-8], is supported by the subjective feeling of a decreased dream activity reported by the majority of patients. In relation to dream emotional content, the results are consistent with previous studies[8,29]: before treatment, approximately 50% of patients were not able to identify a predominant dream emotion, whilst the other 50% prevalently experienced negative emotional content and unpleasant mood. The increased dreams' complexity reported by the majority of patients and generally described as greater plot articulation of dreams and/or as dreams with enhanced number of bizarre elements, finally

agree with the study of Kramer[12] that found in the dreams of depressed patients a lower plausibility compared to a group of organic patients.

Remarkable changes in several dream parameters occurred after the beginning of antidepressant drug therapy.

Concomitantly with the decrease of depressive symptoms severity, the 8-week escitalopram treatment yielded to a significant improvement in the recall of both quantity and quality of dreams and, noteworthy, those patients whit lower clinical benefits kept on reporting impaired dream experiences. Specifically, MADRS and BDI scores remained high in those patients who kept on reporting reduced dream activity, negative dream emotional contents and increased dream complexity. Consistently with these findings, an enhancement of dreaming was previously noted during treatment with SSRIs fluoxetine[5,30] and citalopram[31].

The reported increased dream activity following the therapy with escitalopram may appear paradoxical in relation to the wide literature data indicating a reduction of REM sleep duration during antidepressant treatment. A possible explication may be that a significant proportion of dreams also occurs in non-REM sleep[32-38]. Moreover, patients on antidepressant treatment often show a longer duration of sleep with delayed awakening respect to pretreatment period; since REM activity is more intense during the last part of the sleep, the increased recall of dreams could be mainly related to the recall of this last portion of REM activity[4]. In addition, a cognitive improvement following recovery from depression might be hypothesized to lead to an amelioration in the memory of dreams[39].

The results of the study also indicated that patients on escitalopram treatment showed more clear recall of dream quality, less complex and more emotionally vivid dreams; these data confirm previous findings reported by the majority of authors[29,40-43].

It is known that the study of sleep and circadian functions may help physicians in monitoring the progression of mood disorders[4,44-51]; the results of the present study evidence how the changes in some specific dreaming characteristics, such as the subjective recall of dream activity, the dream recall quality, the dream emotional content and the dream complexity represent reliable markers of the effectiveness of antidepressant therapy such as that with escitalopram. The easiness with which dream experience alterations can be explored during a clinical interview and the relative precocity with which such alterations appear along antidepressant treatment could make them potential valuable clinical markers.

Further investigations carried out on larger samples as well as in double-blind placebo-controlled designs are needed to better clarify the role of dreaming in depression and even in the prediction of remission from depression.

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