

Anxiety, depression and anger suppression in infertile couples: a controlled study

S.Fassino^{1,3}, A.Pierò¹, S.Boggio¹, V.Piccioni² and L.Garzaro¹

¹Department of Neurosciences, Psychiatric Institute and Clinic, University School of Medicine, via Cherasco 15, CAP 10126, Turin and ²Department of Obstetrics and Gynaecology, 'S. Anna' Hospital of Turin, Italy

³To whom correspondence should be addressed. E-mail: secondo.fassino@unito.it

BACKGROUND: Although several authors have suggested an important pathogenic role for psychosocial factors in 'functional' infertility, the extent to which depression, anxiety and expressed emotional patterns correlate to infertility is not yet clear. **METHODS:** This study included 156 infertile couples (recruited at intake) and 80 fertile couples, whose personal characteristics were recorded. They were examined using scales for the evaluation of the degree of psychopathology [Hamilton Anxiety Rating Scale (HAM-A), Hamilton Depression Rating Scale (HAM-D)], and anger expression [State-Trait Anger Expression Inventory (STAXI)]. The 156 infertile couples were then subdivided into groups based on the cause of infertility ('organic', 'functional' or 'undetermined'). The psychometric evaluation was double-blind with respect to the causes of infertility. **RESULTS:** Differences emerged in the degree of psychopathology between 'organic' and 'functional' infertile subjects and fertile controls. In women, logistic regression identified three variables able to predict the diagnosis subtype; these variables are HAM-A, HAM-D, and tendency toward anger suppression. In men, anger did not emerge as a predictor for diagnosis, whereas HAM-A and HAM-D did. **CONCLUSIONS:** The 'functional' infertile subjects of this sample showed particular psychopathological and psychological features, independent from the stress reaction following the identification of the cause of infertility.

Key words: anger/emotional distress/infertility/psychopathology/psychosomatic factors

Introduction

The relationship between emotional distress and infertility has been studied by several authors (Wright *et al.*, 1989; Greil, 1997), but it is clear that attempts to explore the psychological correlates of infertility have produced mixed results. The lack of uniform results in the literature is due to the several methodological problems of such a complex field of investigation (Greil, 1997).

A relevant problem deals with the theoretical model of reference; studies dealing with the psychological features of infertility are based on two contrasting theoretical models that consider psychopathology as a cause for infertility or as a consequence of this disorder respectively. Both of these models have been investigated in descriptive as well as quantitative studies, but these, however, suffer from great methodological flaws (Greil, 1997).

The first model (psychodynamic-oriented) emphasizes the role of psychogenic elements among the causes of infertility ('psychogenic' hypothesis); this model, in its original version, is today rejected by many authors (Greil, 1997), even if some literature evidence does support this hypothesis (Storelu *et al.*, 1993). Recently, some authors have replaced this model with the 'stress hypothesis' (Wasser *et al.*, 1993; Christie, 1994; Wassar, 1994). The stress hypothesis is embraced also by those

who consider infertility as a psychosomatic disorder (Kemeter, 1988; Facchinetti *et al.*, 1992; Gallinelli *et al.*, 2001); they have outlined the impact of emotional states and of the ability of coping with stress (Demyttenaere *et al.*, 1992) on the neuroendocrinological state (Demyttenaere *et al.*, 1994; Hendrick *et al.*, 2000), on pregnancy rates (Domar *et al.*, 1992a), and on treatment outcome for assisted conception (Boivin and Takefman, 1995; Klonoff-Cohen *et al.*, 2001).

Many investigators have also tried to demonstrate a causal link between psychopathology and infertility, but results are contradictory; some authors did not find significant differences (Downey *et al.*, 1989; Downey and McKinney, 1992), whereas others reported greater degrees of interpersonal distrust and maturity fear (Fassino *et al.*, 2002b), anxiety and dissatisfaction (O'Moore *et al.*, 1983; Demyttenaere *et al.*, 1989), depression (Kemeter, 1988), and a tendency toward somatization (Schmidt *et al.*, 1994) in women with 'functional' infertility.

The second model is fostered by those supporting the theory that psychological distress is secondary to infertility. They hold that the experience of infertility imposes profound emotional distress on the individual and the couple (Stoleru *et al.*, 1996; Bringhenti *et al.*, 1997) and underline that this condition is a constant source of psychological (Moller and Fallström, 1991) and social stress (Greil, 1997).

Despite some evidence that depressive symptoms in infertile couples are so common as to reach, in women, a prevalence that is twice that found in the general population (Domar *et al.*, 1992b; Beutel *et al.*, 1999), even in the context of psychological distress, results in the literature are not definitive and consistent (Greil, 1997). In fact, whereas some authors believe that infertile women can be distressed, though not in a clinically significant way (Downey and McKinney, 1992; Bringhenti *et al.*, 1997; Wischmann *et al.*, 2001), others highlight the relevance of psychological consequences such as anxiety (Dhillon *et al.*, 2000; Oddens *et al.*, 1999), depressed mood (Berg and Wilson, 1990), and lower self-esteem (Newton *et al.*, 1999; Oddens *et al.*, 1999).

Thus, at present there is no general agreement about the role of anxious–depressive symptomatology in the pathogenesis and course of infertility. Several descriptive studies in infertile couples suggested a greater susceptibility to anxiety and depression (Dunkel-Schetter and Lobel, 1991; Matsubayashi *et al.*, 2001) as a factor that reduces the ability to conceive (Sanders and Bruce, 1997); however, most of the controlled studies did not find significant differences between infertile couples and fertile controls (Dunkel-Schetter and Lobel, 1991; Wischman *et al.*, 2001).

Moreover, infertile couples often experience strong anger and anxiety, but sometimes these seem to be denied (Chiba *et al.*, 1997) or repressed (Facchinetti *et al.*, 1992). In addition, for anger it is difficult to state whether anger levels and expressions are consequences of the stressful condition experienced by those who do not succeed in conceiving a child or instead are predisposing factors for this condition.

The inability to express anger is typical of psychosomatic disorders (Fava and Sonino, 2000; Fassino *et al.*, 2001) and of those disorders that are expressed through the body, involving important biological repercussions on the organism (Raikkonen *et al.* 1999; Lavoie *et al.*, 2001), even when psychiatric disorders are not evident.

Anger, in its multifaceted nature, has been assessed according to the conceptualization of Spielberger, who stressed the importance of considering anger both as a changeable emotional condition (emotional state) and as a trait (Spielberger, 1996). Trait-anger depends on the frequency of anger experiences, defining the individual's predisposition toward anger. Moreover, Spielberger (1996) emphasized the fact that individuals are very different in the way they suppress or express anger.

For stressors and related emotions, it is important to know that they change according to the duration of infertility; this is another methodological problem (time of observation). There is strong agreement that emotional distress for the infertile couple may arise from the unsuccessful attempts to conceive a baby (Moller and Fallstrom, 1991), as well as from the long diagnostic (Lee *et al.*, 2001) and therapeutic procedures required (Hunt and Monach, 1997; Oddens *et al.*, 1999; Hammarberg *et al.*, 2001).

In particular, many studies underscore that treatments for assisted conception, and particularly IVF, which is the most studied of these, are a source of stress for the couple (Boivin *et al.*, 1995), who make a great emotional investment in these

treatments (Hammarberg *et al.*, 2001). Sadness, depression, anxiety (Slade *et al.*, 1997), hopelessness, and anger (Ardenti *et al.*, 1999) are common in infertile couples undergoing IVF treatment. The emotional distress is particularly great when waiting for treatment outcome (Boivin *et al.*, 1998), in the case of unsuccessful treatment (Newton *et al.*, 1990; Slade *et al.*, 1997) and in the cycles following the first attempt (Boivin *et al.*, 1995); it also depends also on the ability of the couple to cope with this condition (Hynes *et al.*, 1992; Demyttenaere *et al.*, 1998). Moreover, some authors indicate that the outcome of these treatments is also influenced by the degree of anxiety and depression (Thiering *et al.*, 1993; Smeenk *et al.*, 2001) and by negative affect (Bevilacqua *et al.*, 2000).

Other important methodological problems are (Greil, 1997): (i) the greater attention to given to infertile women rather than to the infertile couple, (ii) infertile couples' strong desire for social acceptability through childbearing and the influence of this desire on the answers to self-administered questionnaires (Demyttenaere *et al.*, 1998), (iii) subject selection, (iv) type of control group used, (v) the cross-cultural variation, and (vi) the influence of knowing whether the infertility is due by a male or female factor on the expression of anger in the couple (Demyttenaere *et al.*, 1998).

Notwithstanding the interest shown by several authors, at present little has been written about whether differences exist regarding anxiety, depression, and anger management in couples with certain organic causes of infertility ('organic' infertility) and those with infertility due to certain non-organic causes ('functional' causes). Because these couples are exposed to the same stressor (infertility) the finding of different levels of anxiety, depression and anger might suggest a role of these elements in the pathogenesis of 'functional' infertility.

Considering the recommendations found in the literature bearing on research design, the study was designed on the basis of some methodological and theoretical assumptions: (i) if a 'functional–psychogenic' infertility exists, it may involve a selected group of a small number of couples, otherwise the doubts of several authors on the subject are difficult to explain; (ii) to identify this subgroup and to avoid the risk of overlapping with 'organic' infertility, certain aspects must be considered: (a) couples with a 'functional-psychogenic' infertility were only those with both partners having no certain organic disorder; (b) subjects with minimal or uncertain organic disorders ('undetermined' group) were excluded, even if some of these situations might be correlated to psycho-neuro-endocrinological stress (Demyttenaere *et al.*, 1994); (c) Axis I disorders (DSM-IV) (American Psychiatric Association, 1994) were excluded: they were considered as all the other medical illnesses, including poorly adaptive psychological functioning, which is not necessarily enough to describe a full-syndrome psychiatric disorder; in fact, the normal variation of psychological functioning can significantly influence fertility (Facchinetti *et al.*, 1992); (d) subjects were studied at intake, when they were still unaware of the cause of infertility and did not know which partner was infertile; (e) the study used standardized tests, with strong theoretical bases (e.g. State–Trait Anger Expression Inventory: STAXI) (Spielberger, 1996);

(f) tests evaluated by the interviewer should be used (and the interviewer should be unaware of the causes of infertility).

This study was designed to identify a subgroup of infertile couples in whom psychopathological and psychological elements (particularly with regard to anger management) play a role in the pathogenesis.

The objectives of this study were to verify the possibility of different anxiety and depression levels and anger management in individuals with 'organic' infertility and in those with 'functional' infertility, compared with fertile controls, and to assess psychosocial and symptomatological features independently associated with infertility subtype ('organic' or 'functional').

Materials and methods

Subjects

Two groups of subjects were recruited for this study. The first group included 172 infertile couples recruited from 255 couples consecutively admitted between December 1999 and July 2001 to the outpatient department for diagnosis and care of fertility disturbances at St Anna Hospital in Turin, Italy. Only the couples matching the following inclusion criteria participated in the study: Italian (for the language knowledge), married, aged 18–41 years, first conception attempt (≤ 2 years), not receiving treatment, and not waiting for a treatment for infertility (i.e. no previous diagnosis of infertility). This selection aimed at avoiding the confounding effect that some of these features might have on the assessment of anxiety, depression and anger levels.

Seven couples were excluded because of age, 12 because they had already received treatment for their infertility (four had succeeded in conceiving a child), seven because one of the partners was not Italian, 10 because infertility had lasted >2 years, nine because they had already received a diagnosis of infertility.

Both members of the couple were then interviewed by an expert psychiatrist to assess the presence of Axis I disorders (American Psychiatric Association, 1994). Thirty-two couples with at least one member with an Axis I disorder were then excluded from the study.

The assessment of psychiatric disorders was conducted with the Structured Clinical Interview for DSM-IV (SCID-I) (First *et al.*, 1995). At that point, 32 couples were excluded; two couples were excluded because one member was diagnosed with psychotic symptoms, 12 for major depression, 11 couples for anxiety disorders, and seven couples for eating disorders.

The objective of such selection was to allow the study of the psychological and psychopathological features correlated with infertility, instead of the reproductive disorders of a psychiatric population. Moreover, STAXI scores may be influenced by depressive and psychotic Axis I disorders (Spielberger, 1996).

During the recruitment procedure, six couples refused to take part in the study. Thus, the sample considered eligible for the study included 172 infertile couples (344 subjects). Sixteen couples did not properly complete the psychological test or dropped out during the diagnostic evaluation phase suggested by gynaecologists. Thus, 156 (90.7%) of the 172 couples eligible for the study completed the protocol.

The second group (fertile controls) consisted of 114 fertile couples recruited by public nursery schools in and around the district of Turin during 1999–2001. This group was selected from all available couples between the ages of 18 and 45 years, married, Italian, having at least one child (aged 1–6 years), absence of current clinical psychiatric

disorders (Axis I of DSM-IV), as evaluated with Structured Clinical Interview for DSM-IV Axis I disorders: SCID-NP (not-patient) (First *et al.*, 1995).

The recruited subjects made an appointment with the psychiatrist to be interviewed and to complete the STAXI. Seventy per cent of the eligible couples ($n = 80$ couples) completed the study protocol.

Study design and procedures

The following protocol, including sessions and clinical examinations, was approved by the Institutional Review Board of St Anna Hospital before the study was performed. All subjects were guaranteed anonymity during the data processing phase. All subjects were asked for informed written consent to participate in the study.

Recruitment of infertile couples

The infertile couples were recruited for the study during the assessment phase before the causes of infertility were ascertained (intake). The first contact of the couples was with a specialist in obstetrics and gynaecology. On the same day, each couple was administered the SCID assessment and visited by a psychiatrist who was unaware of the couple's fertility status. In this way, a double-blind procedure between the two specialists was carried out.

Infertility diagnosis

The couples were considered infertile when they had unsuccessfully tried to conceive a child with natural methods for ≥ 1 year. The infertility diagnosis was confirmed within 3 months, after all the subjects had been assessed by gynaecological and andrological clinical examinations, seminal liquid examination, post-coital test, progesterone assay, hysterosalpingography, and, where needed, biopsy of the endometrium and laparoscopy.

The group of infertile subjects was then divided into three sub-groups: the first group ('organic' infertility) included couples whose infertility was due to ascertained organic causes. Infertility was considered due to organic causes when at least one of the clinical examinations was positive in a member of the couple, according to the diagnostic criteria outlined by the Practice Committee of the American Society for Reproductive Medicine (Guzick *et al.*, 1998).

The second group ('functional' infertility) included couples in which both members had negative results for all the examinations performed. In these cases, infertility was defined as 'functional'. The hypothesis is that in such individuals psychological functioning might have a role among the various causes of infertility.

The third group included couples whose results showed physical damage or endocrine anomalies, which were unlikely to result in infertility (Guzick *et al.*, 1998) in one or both of the partners. For men, these anomalies were a spermogram revealing the presence of asthenozoospermia or bradykinesia of a light/mild degree, which was not enough to explain prolonged periods of infertility; for women, almost 50% had mild or unilateral tube damage, ~25% had mild endometriosis, and 25% had other diagnoses (luteal phase deficiency, polycystic ovary, etc.).

In summary, the infertile sample finally included 156 couples of whom 56 couples were in the organic group, 29 couples were in the functional group, and 71 couples were in the undetermined group. The high number of subjects included in the third group can be explained because of the accuracy of the diagnostic assessment, aimed at allowing the identification of a group of functional infertility as definite as possible with respect to the hypothesis of a 'functional-psychogenic' origin.

We excluded this group ('undetermined' group) from further analysis because it was not possible to ascertain for certain whether the cause of infertility was definitely 'organic' or definitely 'functional'.

Several authors have, in fact, underscored that most 'undetermined' infertilities cannot be defined as 'psychogenic' (Demyttenaere *et al.*, 1998).

On the other hand, many authors consider such couples as 'functionally' infertile; however, on the basis of the study objectives, functional infertility was diagnosed only for couples where somatic causes were not ascertained for both partners with the available diagnostic techniques.

Measures

Hamilton Rating Scale for Depression (HAM-D)

The HAM-D is a rating scale for depression, used in its 21-item version (Guy, 1976); it has been widely adopted and has good validity and inter-rater reliability (Cicchetti and Prusoff, 1983). It is a point of reference for all depression scales. The interviewer was adequately trained in the use of the rating scale, to grant good internal consistency (alpha coefficient = 0.92) and interrater reliability (alpha coefficient = 0.93).

The 21 items are rated on either a 5-point (0–4) or 3-point (0–2) scale. In general, the 5-point scale items use a rating of 0 = absent; 1 = doubtful to mild; 2 = mild to moderate; 3 = moderate to severe; 4 = very severe. A rating of 4 is usually reserved for extreme symptoms. The 3-point scale items used a rating of 0 = absent; 1 = probable or mild; 2 = definite. The first 17 items are the most important ones, defining cut-off scores for the severity of depression: >25 severe, 18–24 moderate, 8–17 mild, <7 no depression. The total score is a reliable index of the pervasiveness of depression (Guy, 1976). These features support the use of the HAM-D scale in every diagnostic setting (Hamilton, 1960).

Hamilton Rating Scale for Anxiety (HAM-A)

The HAM-A (Hamilton, 1959) is known and widely used as well as the HAM-D, and these two questionnaires share some items. The HAM-A consists of 14 items, each with a score ranging from 0 (absence) to 4 (very severe). Cut-off scores are as follows: 0–5 no anxiety, 6–14 mild anxiety, >15 severe anxiety. Also the HAM-A is a rating scale that is filled in by the interviewer. The interviewer was adequately trained in the use of this rating scale, which has high internal consistency (coefficient alpha = 0.92), alpha test-retest (= 0.96), and inter-rater reliability (= 0.92).

State-Trait Anger Expression Inventory (STAXI)

The STAXI (Spielberger, 1996) consists of 44 items that are divided into six scales and two subscales. It measures the intensity of anger as an emotional state (State-anger = first 10 items) and the disposition toward anger as a personality trait (Trait-anger). Participants rate themselves on 4-point scales for each item, assessing either the intensity of their angry feelings or the frequency with which anger is experienced, expressed, suppressed, or controlled. In each case, higher scores indicate a greater level of anger and its suppression or expression.

The Trait-anger (items 11–20) scale contains two subscales, T-Anger/T (items 11–13, 16), which measures the general disposition toward angry feelings (angry temperament), and T-Anger/R (items 14, 15, 18, 20), which measures the tendency to express anger when one is criticized (reaction to criticism). Additional scales include Anger Expression-In (AX-IN, items 23, 25, 26, 30, 33, 36, 37, 41), which measures the frequency with which angry feelings are suppressed; Anger Expression-Out (AX-OUT, items 22, 27, 29, 32, 34, 39, 42, 43), which measures the frequency of the expression of anger toward other people or objects in the environment; and Anger Expression-Control (AX-Con, items 21, 24, 28, 31, 35, 38, 40, 44), which measures the frequency of attempting to control the expression

of anger. The final scale, AX/EX (AX-IN + AX-OUT + AX-Con + 16), gives a general index of the expression of anger.

The STAXI has been validated on a variety of normal and clinical populations and has good psychometric properties (Spielberger, 1996).

Statistical analyses

All data analyses were performed using the Statistical Package for Social Sciences (SPSS, 1998). First, the association between the socioeconomic level of the couples and the diagnosis was evaluated ('organic' infertility, 'functional' infertility, and fertility). The association was then verified with the χ^2 -test. Second, a comparison for sociodemographic characteristics (age, educational level) and psychopathological features (HAM-A, HAM-D, STAXI) among the three groups (infertility with 'organic' ascertained causes, infertility with exclusion of organic causes or 'functional' infertility, and fertile controls) was made. This analysis was performed with one-way analysis of variance (ANOVA) and post-hoc *t*-test (Duncan test).

Corrective measures for the post-hoc test (e.g. the Bonferroni correction) were not used for two reasons: (i) cogent arguments against the practice for exploratory studies have been put forward (Rothman, 1986), and (ii) data dredging was avoided by conducting only preplanned analysis (Grove and Andreason, 1982).

Finally, two stepwise logistic (by block method) regressions (women and men separately) attempted to determine the presence, among the variables studied, of independent factors that might discriminate significantly between 'organic' and 'functional' infertility groups.

Results

Descriptive analysis of the sample of infertile couples

The final sample consisted of 156 infertile couples, who were unaware of the causes of their infertility problem at the time they were administered the tests. On the basis of the clinical examinations and the specialist visit, they were subdivided into the three aforesaid groups.

The 56 couples of the organic group included six (10.7%) couples with both partners affected by organic lesions responsible for infertility, 34 (60.7%) couples with male infertility, and 16 (28.6%) with female infertility. The 29 couples of the 'functional' infertility group were all made up of partners free of organic lesions. Last, the 71 couples of the 'undetermined' infertility group included 12 (17%) with an uncertain condition for both partners, 35 (49.3%) with 'undetermined' male and 'functional' female, and 24 (33.7%) with 'undetermined' female and 'functional' male.

Psychosocial characteristics and infertility subtype

The comparison (ANOVA) involved three groups: infertile 'organic' subjects, infertile 'functional' subjects, and fertile subjects. The age, educational level, and results obtained by the three groups of women and corresponding groups of men on the STAXI, HAM-A, and HAM-D subscales are presented in Tables I and II respectively.

The χ^2 -test was used to assess the likelihood of an association among infertility subtype, fertility and the socioeconomic level of the couple. No association emerged when the two groups of infertile women were considered separately (d.f. 4; $\chi^2 = 2.59$; $P < 0.628$, non-significant). In the organic infertility group, 34 (60.7%) couples were middle class, 15 low class (26.8%), and seven high class (12.5%); in the group with

Table I. Comparison of organic infertility, functional infertility, and fertility: the female sample

	OIW (n = 56) A	FIW (n = 29) B	CW (n = 80) C	F ^a	P ^a	Post-hoc ^b
Age	30.89 ± 4.27	29.37 ± 3.70	31.37 ± 4.63	2.22	< 0.111	–
Education level	11.33 ± 3.26	12.82 ± 3.65	12.12 ± 3.44	1.94	< 0.146	–
HAM-A	14.10 ± 1.85	16.34 ± 1.71	4.31 ± 1.99	649.2	< 0.000	C < A, B B > A > C
HAM-D	15.41 ± 1.88	11.72 ± 1.60	3.23 ± 1.70	841.2	< 0.000	C < A, B B < A
STAXI						
S-ANG	11.53 ± 3.12	12.58 ± 3.68	12.81 ± 7.09	0.924	< 0.399	–
T-ANG	13.37 ± 6.24	15.96 ± 6.18	17.45 ± 7.76	5.55	< 0.004	C > A, B
T-ANG/T	11.92 ± 5.04	12.44 ± 7.94	11.32 ± 7.70	0.312	< 0.732	–
T-ANG/R	6.78 ± 2.69	7.68 ± 3.07	6.98 ± 2.62	1.07	< 0.342	–
AX-IN	13.44 ± 2.10	18.48 ± 3.10	17.00 ± 9.24	6.94	< 0.001	B > A, C
AX-OUT	13.21 ± 2.73	15.00 ± 4.39	15.27 ± 4.30	4.95	< 0.008	A < B, C
AX-CON	23.87 ± 4.17	17.68 ± 5.82	21.60 ± 7.76	8.89	< 0.000	A > C > B
AX-EX	21.69 ± 9.11	29.20 ± 11.16	25.97 ± 9.37	6.47	< 0.002	B > C, A

^aF and P value obtained with ANOVA.

^bSignificant post-hoc comparisons (alpha level < 0.05) with Duncan test.

OIW = organic infertile women; FIW = functional infertile women; CW = fertile women; HAM-A = Hamilton Anxiety; HAM-D = Hamilton Depression; STAXI = State-Trait Anger Expression Inventory; S-ANG = intensity of anger as an emotional state; T-ANG = angry temperament; T-ANG/T = general predisposition to feel or express anger without a specific reason; T-ANG/R = tendency to express anger provoked by criticism; AX-IN = suppressed anger; AX/OUT = anger expressed toward other people or objects in the environment; AX/CON = anger control; AX/EX = general index of the expression of anger.

Table II. Comparison of organic infertility, functional infertility, and fertility: the male sample

	OIM (n = 56) A	FIM (n = 29) B	CM (n = 80) C	F ^a	P ^a	Post-hoc ^b
Age	33.69 ± 4.63	31.51 ± 4.46	33.95 ± 5.46	2.60	< 0.078	–
Education level	11.33 ± 3.89	11.79 ± 3.69	13.06 ± 3.51	3.89	< 0.022	C > A, B
HAM-A	11.39 ± 2.32	13.93 ± 1.98	4.48 ± 1.59	348.4	< 0.000	C < A, B B > A
HAM-D	13.75 ± 2.37	9.86 ± 2.27	2.92 ± 1.55	501.3	< 0.000	C < A, B B < A
STAXI						
S-ANG	11.07 ± 1.37	11.51 ± 2.45	11.08 ± 1.74	0.719	< 0.488	–
T-ANG	12.94 ± 6.34	13.68 ± 5.00	15.02 ± 5.33	2.31	< 0.101	–
T-ANG/T	6.21 ± 1.93	6.86 ± 2.79	6.17 ± 2.13	1.11	< 0.330	–
T-ANG/R	10.91 ± 4.02	11.79 ± 8.05	9.63 ± 4.36	2.24	< 0.109	–
AX-IN	16.50 ± 4.12	18.10 ± 3.84	17.62 ± 5.04	1.51	< 0.222	–
AX-OUT	13.51 ± 2.19	14.58 ± 3.35	13.48 ± 2.81	1.89	< 0.153	–
AX-CON	23.58 ± 4.61	22.55 ± 6.10	24.08 ± 5.29	0.923	< 0.399	–
AX-EX	22.28 ± 6.78	25.72 ± 7.73	22.73 ± 8.16	2.11	< 0.124	–

^aF and P value obtained with ANOVA.

^bSignificant post-hoc comparisons (alpha level < 0.05) with Duncan test.

OIM = organic infertile men; FIM = functional infertile men; CM = fertile men; for the other abbreviations, see the Table I.

functional infertility, 20 couples (69%) were middle class, five (17.2%) low class, and four (13.8%) high class. Finally, in the group of fertile couples 54 (67.6%) were middle class, 13 (16.2%) low class, and 13 (16.2%) high class.

Psychological factors associated with ‘organic’ or ‘functional’ infertility

A stepwise logistic regression was designed to determine whether there were predictive variables of ‘functional’ versus

‘organic’ fertility in infertile women. After including personal (educational level, age) and psychopathological variables (HAM-A, HAM-D, STAXI) in different steps, a three-variable model was obtained (HAM-A, HAM-D, AX-IN), which allowed a correct classification of the 97.7% of the cases.

Another stepwise logistic regression was designed to determine whether there were predictors of functional versus organic fertility in infertile men. After including personal (educational level, age) and psychopathological variables

Table III. Stepwise logistic regression: prediction of infertility status in women and men

Gender	Variable	Parameter estimate	χ^2 (Wald)	<i>P</i>	OR	95% CI
Women	HAM-A	1.42	7.44	< 0.0064	4.16	3.54–4.68
	HAM-D	–0.979	6.87	< 0.0087	0.37	0.00–0.74
	AX-IN	1.10	9.85	< 0.0017	3.01	2.66–3.36
Men	HAM-A	1.54	10.15	< 0.0014	4.67	4.19–5.15
	HAM-D	–0.711	15.63	< 0.0001	0.49	0.32–0.66

Stepwise logistic regression: d.f. = 1. Presented are significance level (*P*), the odds ratio (OR) and the 95% confidence intervals (CI) of the significant independent predictors of the binary outcome variable of organic infertility versus functional infertility. For abbreviations see Table I.

(HAM-A, HAM-D, STAXI) in different steps, a two-variable model was obtained (HAM-A, HAM-D), which allowed a correct classification of 89.5% of the cases.

These two models are shown in Table III, along with the significances and odds ratios (OR). In women, higher degrees of anxiety and tendency to anger repression seem to be predictors of ‘functional’ infertility, whereas greater levels of depression seem to predict ‘organic’ infertility (even if in this case the confidence range for OR intersects zero). For men, results are similar (Table III), but the model does not include the tendency to anger repression.

Discussion

This report deals with a subject widely debated in literature, that is, the role psychological functioning plays in infertility. In particular, it was hypothesized that, beyond the common stress reaction associated with the repeated failure of the attempts to conceive a baby, which is well described in the literature (Greil, 1997), there is a greater pre-existing psychological vulnerability in couples who are infertile from functional causes.

First of all, it should be underscored that this study is only in part comparable with others in the literature because of the study design and particularly the double-blind procedure, selection/inclusion criteria, and the exclusion from the statistical analysis of subjects with ‘undetermined’ infertility.

The first objective of the study was the assessment of anxiety, depression, anger, and difficulties in expressing angry feelings, double-blind with respect to the diagnosis of infertility subtype, after reducing the heterogeneity of the infertility sample and distinguishing two subgroups, the first with ascertained organic causes (‘organic’ infertility), the second without (‘functional’ infertility).

Because this comparison entailed the assessment of psychopathological features such as anxiety, depression and anger, the following variables were considered, being generally accepted that they can be associated with different degrees of anxiety, depression and anger in infertile couples (Klock and Maier, 1991; Greil, 1997): age, years of schooling, and socioeconomic levels. Other potential confounding elements (cross-cultural variation, infertility duration, type of factor responsible for infertility, in men or women, previous treatments, etc.) were controlled through the study design.

Regarding the anxious–depressive symptomatology, from

the comparison among the three groups of men and women (‘organic’ infertility, ‘functional’ infertility, and fertility), the following evidence emerged (Tables I and II): (i) anxiety and depression levels are higher in the two groups of infertile subjects than in controls, both in men and women; and (ii) there are differences also between subjects with organic and functional infertility, with the former scoring higher on HAM-D and the latter on HAM-A.

The differences in the anxious–depressive symptomatology between infertile and fertile subjects, which, however, are a little higher than normal baseline when compared with cut-off scores in HAM-A (Hamilton, 1959, 1960) and HAM-D (Guy, 1976), support the findings by some authors (Domar *et al.*, 1992b, 1999; Oddens *et al.*, 1999; Kee *et al.*, 2000; Matsubayashi *et al.*, 2001), but they are not consistent with those obtained by others (Wright *et al.*, 1989; Bringhenti *et al.*, 1997; Wischmann *et al.*, 2001). As already stated by other authors (Greil, 1997; Wischmann *et al.*, 2001), the sample selection, the kind of control group, and the confounding variables in several studies are probably the basis of these differences (Smeenk *et al.*, 2001).

Thus, both men and women with ascertained organic causes scored higher on HAM-D than did those for whom organic causes have been excluded (‘functional’), who instead displayed greater degrees of anxiety (HAM-A). These data will be discussed later, according to the results of the logistic regression.

The comparison of anger among the three groups of men showed differences neither in degrees of anger nor in management of aggressive feelings (Table II). On the other hand, for women, the comparison showed that (i) fertile women have a temperament more inclined to anger than the two groups of infertile women; and (ii) the way anger is expressed is different in the three groups of women such that women with functional infertility experience higher levels of anger, which, however, is often suppressed, whereas women with organic infertility have lower anger levels also with respect to controls (Table I).

Women with an angry temperament seem to have fewer reproductive difficulties. This finding of a more angry temperament in fertile women is difficult to explain, but it is possible that the greater tendency of infertile women toward the expression of negative feelings might protect them from the excessive somatization (Schmidt *et al.*, 1994), which is frequent in infertile women (Facchinetti *et al.*, 1992). In fact, it clearly emerges that women with functional infertility have less

adaptive anger management than fertile women and those with organic infertility; they suppress anger more often and have a lesser control over it. Moreover, infertile women are likely to have a temperament more inclined to passivity, supporting the data obtained from another sample with a different psychometric assessment (Fassino *et al.*, 2002), as described below.

The different results between men and women seem to support the better coping abilities and lower distress about the infertility in men than in women as reported in the literature (Dhillon *et al.*, 2000). It should be mentioned that no differences emerged in age or educational level in the three groups of women, whereas in the men, fertile men displayed a higher educational level than the two groups of infertile men. This result is in contrast with the opinion of many authors who suggest an association of higher educational level and lower reproductive potentialities (Wischmann *et al.*, 2001). However, differences in methods and sampling make it difficult to compare and generalize these results and to make further inferential analyses.

The second objective of the study was to identify variables able to discriminate whether a subject belonged to the group of infertility with organic or functional causes. The use of logistic regression aimed to evaluate which of the differences at the ANOVA between the two groups of infertile subjects were still significant after excluding the internal correlation among the variables considered.

The logistic regression (Table III) identified three variables (HAM-A, HAM-D, AX-IN) in women and two (HAM-A, HAM-D) in men as independent predictors with regard to infertility subtype.

Because patients and therapists did not know *a priori* the causes underlying infertility, it is possible to suggest the hypothesis that, mostly in women with functional infertility, there is a greater psychological vulnerability to stressors linked with the conception of a child, which might predispose to infertility, through anxious-phobic and psychosomatic reactions (Stauber, 1988). This hypothesis seems to be supported by the evidence that the triad of high anxiety, depression and tendency toward anger suppression in infertile women, with anger suppression being peculiar to psychosomatic disorders, is able to predict at 97% (in this sample) the diagnosis of organic or functional infertility.

In women the presence of anxious traits (subthreshold with respect to a full-syndrome anxiety disorder) and the tendency to suppress anger imply a 3–4-fold greater probability to have a diagnosis of ‘functional’ infertility than a diagnosis of ‘organic’ infertility (see OR in Table III). Previous studies on another sample of infertile couples (Fassino *et al.*, 2002) have outlined that the temperamental component of personality, assessed according to a psychobiological model [Temperament and Character Inventory (TCI) (Cloninger *et al.*, 1994)], is able to predict organic infertility versus functional infertility. It is Harm Avoidance, which, according to the authors of TCI, is a psychobiological trait related to the serotonergic system, typical of passive, anxious, and avoiding people, often associated with depressive features (Svrakic *et al.*, 1993). In eating disorders (Fassino *et al.*, 2001), this trait has shown a peculiar correlation with the tendency toward anger suppression (as

evaluated by AX-In, a STAXI subscale). Further studies might explain and support this evidence.

More caution is needed in discussing the data about depression in women; although logistic regression suggests a strong significance of this variable as a predictor for diagnosis, there is an OR whose confidence interval intersects zero.

Also for men, HAM-A seems to be an important independent predictor of functional infertility. Even in this case the data about depression are uncertain, whereas the data about anger lose their significance, and the presence of a greater anxiety psychopathology increases the probability of being a man with ‘functional’ infertility by 5-fold (see OR in Table III). Thus, the importance of anxious symptomatology with respect to infertility is supported; studies on subjects undergoing treatment have demonstrated that anxiety may influence the pregnancy rates (Facchinetti *et al.*, 1997; Smeenk *et al.*, 2001).

Thus, because data in the literature are not consistent, it is clear that many of the results obtained regarding psychopathology in subjects with ‘unexplained’ or ‘idiopathic’ infertility depend on the inclusion/exclusion criteria of the studies and on the study plan and design. This is the reason that sometimes the impressions of clinicians dealing with reproductive disorders, outlining the importance of counselling and psychotherapeutic treatment of couples who require consultation for fertility disorders, are not matched in empirical research by the finding of significant differences (Facchinetti *et al.*, 1992; Wischmann *et al.*, 2001).

Of course, the results obtained in the present study have limits due to the complexity of the subject (Greil, 1997) and cannot be considered definitive. In particular, the accurate selection of the sample, even if necessary for the study design, decreases the possibility of generalizing the results obtained. However, the results do suggest the possibility of identifying a subgroup of infertile subjects where, beyond the distress that is consequent to the failure of repeated attempts to conceive a baby, there is also a poorly adaptive psychological functioning, which is likely to play an important role in the onset and course of functional infertility. For this subgroup, the intervention of a specialist (Stewart *et al.*, 1992; Domar *et al.*, 1999; Kee *et al.*, 2000), targeting specifically the anxious-depressive symptomatology and psychosomatic features, is necessary even without a full-syndrome psychiatric disorder (Axis I of DSM-IV).

If further studies supported this evidence, it would be possible to decide more accurately which couples should be the target of psychological counselling (Boivin *et al.*, 2001), improving the accessibility to these interventions, which are still used by only a few infertile couples (Boivin *et al.*, 1999).

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