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COPING, INEFFECTIVENESS OF COPING AND THE PSYCHOENDOCRINOLOGICAL STRESS RESPONSES DURING *IN-VITRO* FERTILIZATION

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Abstract—The psychoendocrinological stress responses during *in-vitro* fertilization (IVF) and embryo transfer (ET) were investigated in 40 women as a function of a 'coping–ineffectiveness of coping' construct.

The results demonstrate an important dissociation between emotional and endocrine stress responses and the existence of relatively independent dimensions of arousal (emotional, prolactin, cortisol).

The emotional stress response, i.e. state anxiety levels, are for 34–59% predicted by chronic ineffectiveness of coping, and this both before (anticipation) and after (recovery) the stress of oocyte retrieval (OR) and embryo transfer.

The effect of anticipatory stress, i.e. in the follicular phase and before oocyte retrieval or embryo transfer, on prolactin and cortisol release is more important in women with a high chronic ineffectiveness of coping while the effect of oocyte retrieval itself is more important in women who are effective copers. Other prolactin concentrations, i.e. after OR or ET, are for 14 26% predicted by low palliative coping and high avoiding. Other cortisol concentrations, i.e. after OR or ET, are for 13–19% predicted by comforting ideas.

The advantages of this 'coping–ineffectiveness of coping' construct are weighed against the 'effectiveness of defenses' construct described by Wolff *et al. Psychosom Med* 1964; **26:** 406–413.

It is suggested that these personality dependent stress responses are important for conception rates in spontaneous cycles as well as in stimulated cycles.

INTRODUCTION

IT IS well established that many endocrine systems respond to stress [1]. Stress was supposed to be a nonspecific response of the body to any demand. Indeed, the original stress paradigm was that any kind of stressor provokes in any kind of person the same response [2]. This response was believed to be dependent only on the time a stressor could influence the system. Recent research, however, demonstrated that different stressors (e.g. physical or psychological) can result in different responses [3]. We recently demonstrated that the psychological mechanism of anticipation already determines what will be the effect of the stressor [4]. It was also demonstrated that in the stress response, there can be a dissociation between emotional and endocrine states [5]. It was suggested that this could be due to the difference between so-called sensitizers and so-called repressors which are believed to present respectively exaggerated emotional and exaggerated physiological responses [6]. The use of social

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desirability scales was suggested to overcome this discrepancy between emotional and endocrine responses [7].

It was also demonstrated that in the stress response, a dissociation between the different endocrine systems often occurs [4]. It was suggested that different parts of the endocrinological stress response are related to specific psychological stressors (catecholamines linked to performance, testosterone to gender role) or to effectiveness of psychological functioning (cortisol to ineffectiveness of defenses) [8].

Coping mechanisms are believed to be essential in psychological functioning [9]. Current stress and coping research focus primarily on the stress-reducing effects of coping. While coping may indeed reduce stress, the implementation of a coping strategy may also serve as a source of stress and thus may activate some dimensions of the stress response. We previously demonstrated that anticipatory activation is different in the several endocrine and emotional dimensions of the stress response and that this activation depends as well on the importance of the stressor as on the trait anxiety level of the woman [4].

Although it is well established that infertility is indeed an extremely stressful life event, psychoendocrine studies investigating the stress of infertility (treatment) are not available. *In-vitro* fertilization (IVF) and embryo transfer (ET) are often experienced as a treatment of a last resort [10]. The loss of control, seen by most patients as infertility's most stressful dimension, left them vulnerable to the intense stresses of IVF, less able to handle its multiple demands. Oocyte retrieval (OR) and embryo transfer (ET) are two of the most emotional stages in IVF cycles [10, 11]. Oocyte retrieval is a mechanical ovulation and even when performed by ultrasonography, it remains a physical stressor often requiring anesthetic drugs. Oocyte retrieval is also a psychological stressor: both doctors and patients realize that failure to retrieve an egg precludes all chances for success. Embryo transfer is a mainly emotional stressor and is often experienced beyond the control of her own and of her doctor. Emotions are especially tense and balance between feeling pregnant for a brief moment and feeling the 'babies' may be falling out [10].

The psychoendocrinological responses associated with these stressors are not well documented in the literature.

Therefore, the present study was undertaken and the emotional response, i.e. state anxiety and the endocrine responses, i.e. prolactin and cortisol, to the stress of oocyte retrieval and embryo transfer were investigated.

METHODS

Subjects

Women attending the infertility clinic of the Leuven University Hospital Gasthuisberg for IVF were invited to participate. The first 40 positive responders out of 80 consecutively invited women actually participated.

The average age of the women was 32.4 yr (SD = 4.1) and their infertility had lasted for 6.1 yr (SD = 3.3).

The main indication for IVF was severe male subfertility ($N = 11$), severe mechanical infertility of the woman ($N = 10$), both combined ($N = 6$) and a group comprising women with unexplained infertility, minimal endometriosis (AFS I), and luteal phase insufficiency ($N = 13$). The latter group will be labeled 'insufficiently explained' infertility. The four groups were comparable for age and duration of infertility.

It was the first IVF-cycle for 17 couples, the second for 14, the third for 2, the fourth for 4 and the fifth for 3.

Ovulation induction was initiated on the third day of the cycle in all women with six times 100 μg gonadotropin-releasing hormone agonist (GnRH-a, Buserelin®) intranasally and three ampules of HMG

(Humegon®) daily. Human chorionic gonadotropin (hCG, Pregnyl® 10 000 IU) was given when at least two follicles had reached a diameter of more than 16 mm, and the 17β-estradiol (E_2) concentration was higher than 600 pg/ml. Half an hour before oocyte retrieval, an intramuscular injection of an anesthetic drug (20 mg piritramide, Dipidolor®). Oocyte retrieval ($N = 40$) was performed under vaginal ultrasound guidance, 36 hr later. Inseminated oocytes were incubated for 38–40 hr, at which time cleaved embryos were transferred into the uterus. Up to three embryos were replaced per patient ($N = 28$), extra embryos were cryopreserved. All oocyte retrievals were performed in the morning, all embryo transfers in the afternoon.

Psychometric tests

A Dutch translation of the Zung Depression Scale was used to evaluate depression. When the index (a standardized transformation of the raw score) is equal or greater than 50, there is depressive disorder [12].

The 'Utrechtse Coping Vragenlijst' (UCL) is a Dutch adaptation of the Westbrook Coping Scale and was used to evaluate different coping strategies: active coping, palliative reactions, avoiding reactions, social support seeking, depressive–regressive coping, expression of emotions or anger and comforting ideas. The test–retest reliability in women ranges from 0.76 to 0.43 after 6 weeks [13].

The 'Amsterdamse Biografische Vragenlijst' (ABV-B) is an adaptation of the Eysenck Personality Inventory and was used to evaluate neuroticism (N), neurosomaticism (NS), extraversion (E), and self defensiveness or test attitude (T). The test–retest reliability in women after 3 wk is 0.70 for N, 0.80 for NS, 0.83 for T and 0.87 for E. Results are listed in percentile scores [14].

A Dutch translation of the Spielberger State Trait Anxiety Inventory (STAI) was used to evaluate trait and state anxiety. 'Trait' anxiety is defined as the general tendency of an individual to be upset in stressful situations, or as the mean level of anxiety over a longer period. It is considered as a personality trait. The test–retest reliability ranges from 0.92 (after 1.5 hr) to 0.75 (after 118 days) [15]. 'State' anxiety is defined as the momentarily experienced anxiety.

Study design

The personality questionnaires (trait anxiety, ABV-B, UCL and Zung Depression Scale) were administered in the early follicular phase, i.e. immediately after the first visit to the clinic during this IVF-cycle (day 4–5).

At the same time, i.e. in the early follicular phase, and 4 days later, i.e. in the mid-follicular phase, a blood sample was taken assaying prolactin (PRL) and cortisol concentration. The psychoendocrinological stress response during oocyte retrieval and embryo transfer was studied as follows. Repetitive blood sampling was performed at 30-min intervals using an indwelling catheter. Samples were collected 90, 60 and 30 min before, just before, immediately after and 30, 60, 90 and 120 min after oocyte retrieval or embryo transfer. They were all analyzed for PRL and cortisol. The state anxiety level fluctuates very quickly and was measured once in the early follicular phase and three times during OR and ET, i.e. 90 min before, immediately before and 120 min after.

Radioimmunoassay methods

Prolactin concentrations were assayed using the PRL kits of Medgenix (Institute for radioactive elements, Fleurus, Belgium). Cortisol concentrations were assayed as described previously [16].

Statistical methods

Means $\pm$ standard deviation (SD) are listed unless indicated otherwise.

Kendall Tau coefficients were used as rank-order measures of association between psychometric variables, and between psychometric variables and hormone concentrations. Since hormonal data have a non-Gaussian distribution, logarithmic transformation was performed before analysis of variance and before logistic regression analysis were applicated. Differences in psychometric variables depending on the etiology of infertility were estimated by one-way analysis of variance (anova; F-values and p-values are listed).

The prediction models for emotional variables or hormone concentrations were constructed by logistic regression analysis using a stepwise forward procedure; this procedure first chooses the most predictive variable, then the second one, etc. For all significant predictive variables, R^2 and p-value of the constructed model are listed.

Initially, all psychometric variables were included in the regression analysis. Since the coping mechanisms and the Zung depression score were always selected in the models constructed, we limited the variables to coping and Zung. This selection is moreover logical since the seven coping mechanisms can be used effectively or ineffectively to reduce stress. The Zung depression score can be considered as an indicator of chronic ineffectiveness of coping. Since depression can be considered as an exhaustion, i.e. depression occurs when an individual's coping mechanisms are ineffective in handling the long-term

TABLE I.—PSYCHOMETRIC VARIABLES IN THE INVESTIGATED WOMEN (MEANS ± SD), FOR COMPARISON, THE MEANS OF THE GENERAL POPULATION ARE LISTED

Zung depression	36	46.0 ± 9.4
Trait anxiety	36	40.0 ± 10.1
Neuroticism	50	62.5 ± 28.0
Active coping	16–18	17.8 ± 3.4
Palliative coping	13–18	17.9 ± 3.2
Avoiding	12–16	15.0 ± 3.3
Social support seeking	10–14	13.8 ± 3.7
Depressive coping	10–12	11.1 ± 2.5
Expression of emotion	6–8	6.1 ± 1.9
Comforting ideas	11–14	13.5 ± 2.8

stress of infertility. The construct with the seven coping mechanisms and the Zung depression score will further be labeled as 'coping–ineffectiveness of coping' construct. A limitation of the number of variables was moreover necessitated by statistical limitations due to the small number of observations. Since there is considerable overlap between several psychometric variables (trait anxiety, Zung depression score, neuroticism, neurosomaticism and Body Mass Index—cf. infra), it was logical to include only one of these variables in the predictive models.

RESULTS

The psychometric test results are listed in Table I and demonstrate that the coping in the investigated women is comparable with the one found in a general population. Zung depression score, trait anxiety and neuroticism are, however, higher than in a general population ($p < 0.0001$, $p < 0.05$ and $p < 0.01$ respectively) and they are highly intercorrelated (Fig. 1). It is further positively correlated with neurosomaticism ($\tau = 0.34$; $p < 0.01$) and negatively with extraversion ($\tau = -0.25$; $p = 0.02$).

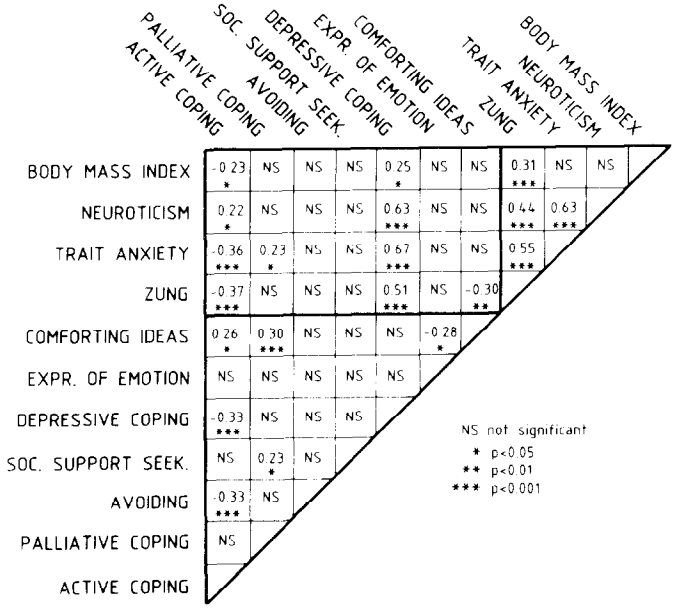

FIG. 1. Kendall-Tau correlation coefficients between coping mechanisms (UCL) and several indicators of ineffectiveness of coping (Zung, trait anxiety, neuroticism and BMI).

In the UCL, the Zung depression score is positively correlated with depressive coping and negatively with active coping and with comforting ideas (Fig. 1). The Zung depression score is not significantly correlated with the duration of infertility nor with the number of previous IVF attempts.

The age of the woman is negatively correlated with the Zung depression score ($\tau = -0.35$; $p = 0.002$), avoiding ($\tau = -0.33$; $p = 0.005$), depressive coping ($\tau = -0.27$; $p = 0.02$) but positively with active coping ($\tau = 0.37$; $p = 0.001$). Duration of infertility is not correlated with either of the psychometric test characteristics.

The psychometric test results were not significantly different in the group of women with mainly male subfertility, mainly female mechanical infertility, combined subfertility or mainly insufficiently unexplained subfertility.

State anxiety during oocyte retrieval and embryo transfer

The state anxiety levels are high in the follicular phase, high before OR and ET but low after OR and ET (Fig. 2). The mean state anxiety level in the early follicular phase is decile seven. The state anxiety evolution during oocyte retrieval and embryo transfer is analogous, although the levels are lower during ET. State anxiety is decile eight 90 min before, decile seven immediately before and decile four 120 min after oocyte retrieval. State anxiety is decile six 90 min before, decile six immediately before and decile four 120 min after embryo transfer.

The age of the woman is negatively correlated with the state anxiety level in the early follicular phase ($\tau = -0.30$; $p = 0.01$) and 90 min before OR ($\tau = -0.27$; $p = 0.01$). The duration of infertility is not correlated with state anxiety levels. The number of previous IVF attempts is negatively correlated with the state anxiety level but only 120 min after oocyte retrieval ($\tau = -0.26$; $p = 0.04$) and 120 min after embryo transfer ($\tau = -0.35$; $p = 0.01$).

Variation in state anxiety levels was predicted by the 'coping–ineffectiveness of coping' model. The regression analysis demonstrates that the Zung depression score is the first predictor for all state anxiety measurements. A higher Zung depression score predicts higher state anxiety levels: in the early follicular phase ($R^2 = 0.50$; $p = 0.0001$); 90 min before ($R^2 = 0.35$; $p = 0.0001$), just before ($R^2 = 0.33$; $p = 0.001$)

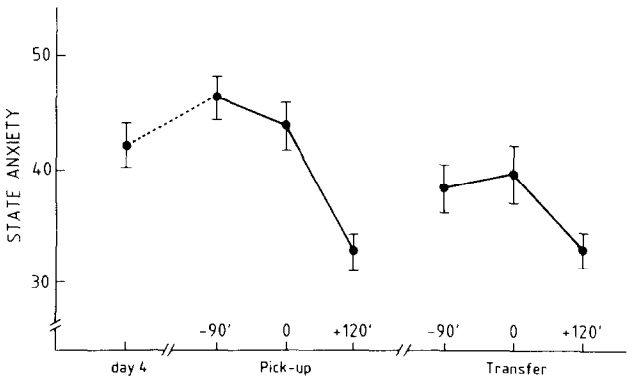

FIG. 2. State anxiety levels in the early follicular phase, during oocyte retrieval and during embryo transfer.

and 120 min after ($R^2 = 0.33$; $p = 0.0001$) oocyte retrieval; 90 min before ($R^2 = 0.59$; $p = 0.0001$), just before ($R^2 = 0.34$; $p = 0.0009$), and 120 min after ($R^2 = 0.41$; $p = 0.0002$) embryo transfer. It can be noted that the difference in state anxiety between the early follicular phase and 90 min before OR is negatively predicted by the Zung depression score ($R^2 = 0.16$; $p = 0.03$). It can also be noted that the difference in state anxiety between 90 min before oocyte retrieval and 90 min before embryo transfer is negatively predicted by the Zung depression score ($R^2 = 0.15$; $p = 0.03$).

Prolactin concentrations during oocyte retrieval and embryo transfer

Prolactin concentrations are low in the early follicular phase but an anticipatory increase in PRL concentrations exists before OR (Fig. 3). The physical stress of OR itself induces a further increase. Before ET, there is no anticipatory incease in PRL concentrations and ET itself has no significant effect on PRL concentrations.

The age of the woman, the BMI, the duration of infertility and the number of previous IVF attempts are not significantly correlated with PRL concentrations.

Variation in PRL concentration was predicted by the 'coping–ineffectiveness of coping' model. For PRL concentrations in the early and mid-follicular phase, this does not lead to a significant model.

During oocyte retrieval and embryo transfer, however, variation in single PRL concentrations can partly but significantly be predicted by the 'coping–ineffectiveness of coping' model (Table II).

Palliative coping is the main predictor for low PRL levels while avoiding is the main predictor for high PRL levels. Social support seeking and the Zung depression score add predictive value to higher PRL levels.

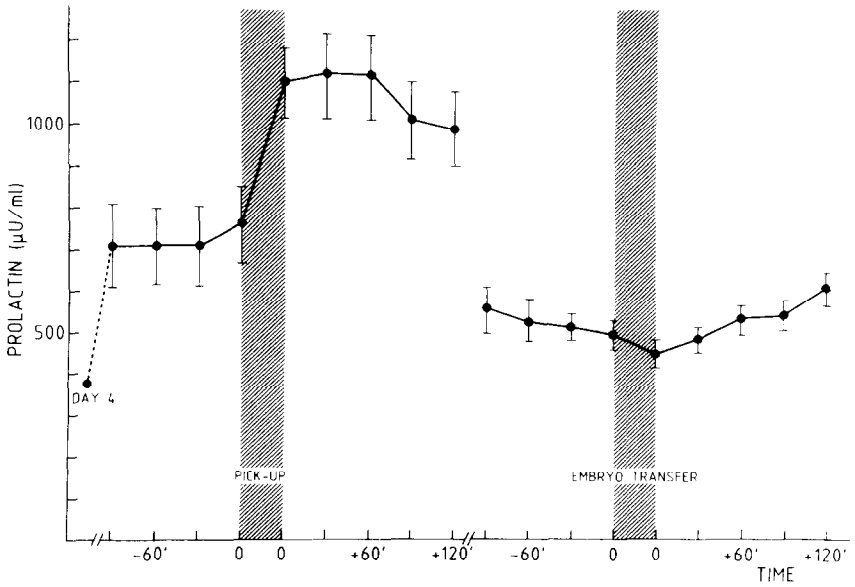

FIG. 3. Prolactin concentrations in the early follicular phase, during oocyte retrieval and during embryo transfer.

TABLE II.—PREDICTION OF PRL CONCENTRATION BY LINEAR REGRESSION (FORWARD STEPWISE PROCEDURE)

PRL 90 min before OR	Zung + $R^2 = 0.11$ $p = 0.04$			
PRL immediately after OR	Palliative coping − $R^2 = 0.09$ $p = 0.05$	Avoiding + $R^2 = 0.14$ $p = 0.06$	Social support seeking + $R^2 = 0.20$ $p = 0.03$	
PRL 120 min after OR	Avoiding + $R^2 = 0.07$ $p = 0.09$	Palliative coping − $R^2 = 0.15$ $p = 0.05$		
PRL 90 min before OR	Avoiding + $R^2 = 0.10$ $p = 0.13$	Palliative coping − $R^2 = 0.24$ $p = 0.07$		
PRL immediately after ET	Palliative coping − $R^2 = 0.10$ $p = 0.08$	Zung + $R^2 = 0.21$ $p = 0.04$	Avoiding + $R^2 = 0.26$ $p = 0.05$	Social support + $R^2 = 0.25$ $p = 0.02$
PRL 120 min after ET	Palliative coping − $R^2 = 0.15$ $p = 0.03$	Avoiding + $R^2 = 0.26$ $p = 0.02$	Zung + $R^2 = 0.33$ $p = 0.01$	Social support + $R^2 = 0.39$ $p = 0.01$

With Zung depression score and coping mechanisms (R^2 = predictability, p = significance level of total model, + denotes positive relationship, − denotes negative relationship).

Cortisol concentrations during oocyte retrieval and embryo transfer

An important anticipatory increase in cortisol concentration exists in the early follicular phase, before OR and before ET (Fig. 4). During OR and ET, there is a gradual decrease in cortisol concentrations for at least

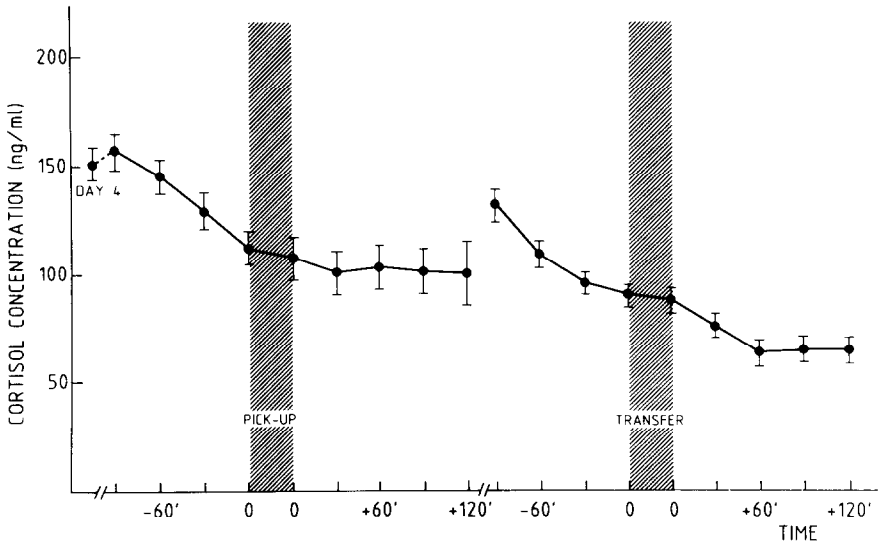

FIG. 4. Cortisol concentrations in the early follicular phase, during oocyte retrieval and during embryo transfer.

the next 2 hr. The physical stress of OR does not seem to influence this decrease.

The age of the woman, the BMI, the duration of infertility and the number of previous IVF attempts are not significantly correlated with cortisol concentrations.

Variation in cortisol concentration was predicted by the 'coping–ineffectiveness of coping' model (Table III). Zung depression score and active coping are the main predictors for high anticipatory cortisol levels. Comforting ideas as a coping mechanism is predictive for high cortisol levels after OR/ET.

It should be noted that the decrease in cortisol concentration between immediately after and 120 min after ET can be significantly predicted by the Zung depression score. After ET, a high Zung depression score predicts a further decrease of cortisol concentrations.

DISCUSSION

Our data demonstrate that the coping mechanisms used by the women in our research group are comparable with those used by a standard population.

The women in our research group are, however, more depressed, more neurotic and more anxious. Our data suggest that women with a high active coping and with comforting ideas as a coping mechanism tend to be depressed less easily; while women with a high depressive coping tend to be depressed more easily.

The finding that women with a high Zung depression score also present a high trait anxiety level, or neuroticism score, or BMI is logical since they all can be considered

TABLE III.—PREDICTION OF CORTISOL CONCENTRATION BY LINEAR REGRESSION (FORWARD STEPWISE PROCEDURE)

Cortisol early follicular	Zung + $R^2 = 0.07$ $p = 0.08$	Active coping + $R^2 = 0.13$ $p = 0.06$	
Cortisol mid. follicular	Active coping + $R^2 = 0.10$ $p = 0.06$	Zung + $R^2 = 0.21$ $p = 0.02$	
Cortisol 90 min before OR	Active coping + $R^2 = 0.05$ $p = 0.18$	Zung + $R^2 = 0.15$ $p = 0.06$	Comfort ideas − $R^2 = 0.19$ $p = 0.07$
Cortisol immediately after OR	Comfort ideas + $R^2 = 0.13$ $p = 0.05$		
Cortisol 120 min after ET	Comfort ideas + $R^2 = 0.19$ $p = 0.01$	Social support + $R^2 = 0.24$ $p = 0.02$	
Decrease in cortisol concentration between immediately after and 120 min after ET	Zung + $R^2 = 0.20$ $p = 0.02$		

With Zung depression score and coping mechanisms (R^2 = predictability, p = significance level of total model, + denotes positive relationship, − denotes negative relationship).

as dimensions of ineffectiveness of coping. The theoretical concept of Spielbergers State Trait Anxiety indeed defines trait anxiety as a characteristic predisposing an individual to present high state anxiety in stressful situations [15]. Neuroticism, at least as measured by the ABV-B, mainly scores behavioural aspects of ineffective coping [14]. The BMI scores the alimentary behaviour which can also be considered as a dimension of chronic ineffectiveness of coping. Giving up of control on food intake, carbohydrate craving, impaired physical exercise indeed can be equivalents of depressive mood shifts.

The observation that older women have a lower Zung depression score, avoiding and depressive coping and a higher active coping should be interpreted carefully. In a general population, these correlations do not exist. Moreover, the duration of infertility does not correlate significantly with any psychometric variable. Our data demonstrate that the older the woman is when participating in IVF-ET and in our experiment, the more emotionally normal she is. We hypothesize two possible mechanisms for this finding.

First, it could well be that all older women participating in IVF-ET are more emotionally stable when compared to younger women. Since indeed the duration of infertility is not correlated with any psychometric variable we speculate that mainly the emotionally normal older women decide for IVF-ET. It is indeed well known in western societies that professionally active and ambitious women conceive at a later age. Older women with a wish for a child (when compared with younger ones and matched for duration of infertility) could thus be more active copers and be less trait anxious. Secondly, it could well be that only the older women participating in our experiment are more emotionally stable and thus that the selection bias is situated in the positive versus negative responders. One could imagine that older women know themselves that their age could be judged negatively ('Why still wishing for a child at this age?') so that only the more motivated (more emotionally normal women) enter our research project.

The latter finding does warn for conclusions on psychometric data on IVF patients in general since only 50% of the women invited participated in the experiment. One further reason is that the test results may reflect a response bias to present as 'normal' subjects in order to be kept on the IVF programme.

Women with previous IVF attempts have a more efficient emotional recovery both after OR and after ET. The emotional anticipation of OR and ET is not influenced by previous IVF attempts. It is important to notice that hormone concentrations are not, even not after OR and ET, influenced by the number of previous IVF attempts. It has been documented earlier that psychological habituation indeed can occur without physiological adaptation [17]. Our data suggest that psychological adaptation mainly exists for recovery but this should be interpreted cautiously since for 17 couples out of 40, it was the first IVF attempt.

The psychological, i.e. state anxiety, and endocrinological, i.e. prolactin, cortisol and testosterone, stress responses were analysed with a 'coping–ineffectiveness of coping' construct. Coping mechanisms are used in order to reduce the harmful effects of stress which can be psychological or biological. The coping mechanisms themselves can, however, also activate some dimensions of the stress response.

We also stated that some coping mechanisms, i.e. active coping or comforting ideas, are more effective than others, i.e. depressive coping. This leads to the notions 'chronic and acute ineffectiveness of coping'.

We propose the Zung depression score (as well as trait anxiety, neuroticism or the BMI) as an indicator of 'chronic ineffectiveness of coping'. Indeed, long-term infertility leads to depression in women with less effective coping mechanisms. This illustrates the well known concept of 'person specificity' in stress research: the same stressor (long-term infertility) results in a depressive mood shift but only in 'some' persons, i.e. in persons with less effective coping mechanisms.

The state anxiety stress response during OR and ET can be regarded as the indicators of the acute ineffectiveness of the used coping strategies. It is thus logical that in the acute stress situation of OR and ET, women with a high Zung depression score also have high state anxiety levels. Indeed, one easily accepts that a chronic ineffectiveness of coping with the infertility problem in general will result in an acute ineffectiveness of coping with the specific stress of OR and ET. When we take into account that oocyte retrieval is a physical and a major emotional stressor while embryo transfer is mainly a minor emotional stressor, it becomes interesting to notice that women with a high Zung depression score are highly state anxious both before OR and before ET while women with a low Zung depression are high state anxious only before OR.

High depressive women are thus ineffective copers in the anticipation of both OR and ET, while low depressed women are thus only ineffective in the anticipation of OR.

It makes sense to be an ineffective coper before OR (How many oocytes they can pick-up, is their quality good, what will be the fertilization rate? . . .), it makes less sense to be an ineffective coper before ET (Shall I feel pregnant for a couple of weeks? I hope the babies will not fall out . . .). High depressive women thus present ineffective coping in the early follicular phase, before OR and ET.

The endocrine stress responses to OR and ET can also be analyzed in function of the 'coping ineffectiveness of coping' construct.

Tonic PRL concentrations are significantly predicted by coping mechanisms: women with high avoiding and low palliative coping have higher PRL concentrations. A high PRL concentration in the anticipation of OR can, on the contrary, be interpreted as 'ineffective coping' since it is predicted by the Zung depression score, i.e. the 'chronic ineffectiveness of coping'. An important increase in PRL concentrations during OR occurs only in women who were effective in coping with anticipatory stress before OR.

This abrupt increase is probably provoked by the physical stress of OR rather than by the emotional stress [18]. Although it is well established that PRL levels rise during stress, very little is known as yet about the specific psychological mechanisms which influence such responses, particularly in human subjects. The studies which investigated PRL stress responses are conflicting and we suggested that this is mainly due to the absence of anticipatory measurements and to the fact that personality characteristics were not taken into account [4].

Anticipatory cortisol concentrations are high in women with a high Zung depression score and a high active coping, i.e. in women with a high active coping although they are depressed or women who are depressed although their active

coping. Clinical experience indeed learns that the psychometric score 'active coping' cannot by itself differentiate between adaptive 'active coping' (facing a problem, looking at it from different point of views, tackling a problem, deciding to start and to stop to face a problem . . .) and maladaptive 'active coping' (infinitely trying again even when it no longer makes sense, never deciding to stop and going on 'forever' . . . which is much more in accordance with monothematic thoughts/acts found in depressive disorders) which can be illustrated by the Greek myth of Sisyphus.

We suggest that especially in the latter group, the Sisyphus-like women, cortisol levels are high. The infertility clinic indeed finds that some patients (the more depressed ones) never give up, would go on for new IVF cycles as long as the doctors agree, and this attitude of failing decision making is rather the expression of depression (no longer capable of taking decisions and thus going on) than of enthusiastic motivation.

Our findings are in accordance with the literature, where cortisol indeed has been described as a sensitive anticipation hormone as well as an indicator of ineffective defenses [19, 20].

The proposed 'coping–ineffectiveness of coping' construct thus results in significant models for state anxiety, PRL and cortisol. The proposed 'coping–ineffectiveness of coping' construct is a simplified adaptation of the 'effectiveness of defenses' construct defined by Wolff *et al.* [21] and offers several advantages.

First, the construct defined by Wolff *et al.* was very complex, including an affect criterion, a function criterion and a defensive reserve criterion. Other authors already demonstrated that it was mainly the affect criterion which was well correlated with physiological reactions [22]. Moreover, this affect criterion is difficult to handle scientifically since it measures the clinically assessed deviation from an individual's typical emotional status. The infertility situation, where couples have faced their unfulfilled wish for a child for years (6.1 yr in our research group), makes it very difficult to assess a person's typical emotional status.

Second, it has been demonstrated that controlling for body size was important in assessing the correlation between 'effectiveness of defenses' and cortisol concentrations [23]. This is very logical since we propose that as well as the Zung depression score as the trait anxiety level, the BMI and the neuroticism score are all dimensions of chronic ineffectiveness of coping. It was indeed recently demonstrated that there is a modest association between cortisol excretion and neuroticism, the dimension of Eysenck's model which is most similar conceptually to our 'chronic ineffectiveness of coping' [24, 25].

Our 'coping–ineffectiveness of coping' thus has several advantages. However, the number of investigated subjects in this study was rather low and many correlations are only borderline significant. Further research is needed to validate the usefulness of the presently proposed construct.

The present investigation, illustrating the use of the 'coping–ineffectiveness of coping' concept in the study of stress responses in stimulated cycles, is important for stress and fertility research. We previously demonstrated that personality characteristics influence conception rates at least in spontaneous cycles [26]. The present study demonstrates that PRL and cortisol concentrations vary with personality characteristics. The clinical importance of these findings is not yet clear.

The literature provides several arguments that PRL and cortisol can interfere with oocyte quality, quantity and fertilization rates.

It has indeed been documented that PRL and cortisol concentrations in serum as well as in follicular fluid are higher in gonadotropin-treated women than in spontaneous cycles [27, 28]. It was also shown that laparoscopic oocyte retrieval results in a 2- to 50-fold elevation of plasma PRL levels apparently without effect on IVF or embryonic development [29]. It is important to notice that in the same study, although not significant, the incidence of pregnancy was highest in the group of patients with the lowest preanesthetic plasma PRL levels. Follicular fluid cortisol levels were found to be higher in stimulated than in spontaneous cycles and they negatively influence fertilization rates [28].

In conclusion, the present data demonstrate that there are several, relatively independent dimensions, i.e. state anxiety levels, PRL and cortisol concentrations, of the stress response during OR and ET.

A 'coping–ineffectiveness of coping' construct is proposed to understand these stress responses, which are important for stress research as well as for fertility research since the investigated hormones are known to influence the outcome of IVF treatment.

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