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G. Wagner, M. Haidvogl, F. Fernandez-  
Aranda, R. Castro, S. Jiménez-Murcia,  
M. Anderluh, et al.**

**Cognitive Therapy and Research**

ISSN 0147-5916

Cogn Ther Res

DOI 10.1007/s10608-012-9518-8



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## Maternal Anxiety, Overprotection and Anxious Personality as Risk Factors for Eating Disorder: A Sister Pair Study

E. Taborelli · I. Krug · A. Karwautz · G. Wagner · M. Haidvogl ·  
F. Fernandez-Aranda · R. Castro · S. Jiménez-Murcia · M. Anderluh ·  
D. Collier · J. L. Treasure · N. Micali

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**Abstract** Using a sister-pair design, we aimed to investigate the role of maternal anxiety in pregnancy and parental overprotection as risk factors for anorexia nervosa (AN) and bulimia nervosa (BN). We were also interested in investigating anxious personality traits in patients with AN and BN compared to their healthy sisters, and their possible association to overprotection. One-hundred-and-fifty-seven females (AN = 94; BN = 63) and their healthy sisters from four European centres were recruited. Data on temperament and childhood characteristics were obtained from cases and their sisters using the Temperament and Character Interview Revised (TCI-R) and the Oxford Risk Factor Interview (ORFI); maternal anxiety and overprotection were obtained from retrospective parental report. Both AN and BN women

displayed significantly higher levels of separation anxiety in childhood in comparison to their sisters, but only women with AN showed anxious temperamental traits. Mothers of women with AN reported higher levels of anxiety during the index pregnancy ( $p < .01$ ), compared to when pregnant with the healthy daughter. The age in months at which women with AN were first left with another adult for a night was also higher compared to their sisters (respectively medians: 12 (range 1–120), 9 (range 1–96),  $p < .05$ ). This was not the case for women with BN. Maternal overprotection was not associated with index daughter temperament. This finding is suggestive of an association between AN and maternal stress and anxiety in utero and later overprotective care, whilst BN was not associated with maternal anxiety or overprotection.

**Keywords** Eating disorders · Anorexia nervosa · Bulimia nervosa · Separation anxiety · Temperament · Maternal anxiety · Overprotection

This work is produced by Dr. Nadia Micali under the terms of a Clinician Scientist Award issued by the NIHR. The views and opinions expressed in this publication are those of the authors and do not necessarily reflect those of the National Health Service (NHS), NIHR or the DH.

E. Taborelli (✉) · N. Micali  
Behavioural and Brain Sciences Unit, UCL Institute of Child Health, 4th Floor, 30 Guilford Street, London WC1N 1EH, UK  
e-mail: e.taborelli@ucl.ac.uk

I. Krug · J. L. Treasure  
Eating Disorders Research Unit, King's College London, London, UK

A. Karwautz · G. Wagner · M. Haidvogl  
Eating Disorders Unit, Department of Child and Adolescent Psychiatry, Medical University of Vienna, Vienna, Austria

F. Fernandez-Aranda · R. Castro · S. Jiménez-Murcia  
Department of Psychiatry, University Hospital of Bellvitge-IDIBELL and CIBER Fisiología Obesidad y Nutrición (CIBEROBN), Barcelona, Spain

M. Anderluh  
Child Psychiatry Unit, University Children's Hospital, University Medical Centre Ljubljana, Ljubljana, Slovenia

D. Collier  
Social, Genetic and Developmental Psychiatry Centre (SGDP), Institute of Psychiatry, King's College London, London, UK

## Anxiety and Eating Disorders

A large body of literature has highlighted the relationship between eating disorders (ED) and anxiety disorders (AD). In particular, anxiety disorders are significantly more prevalent in subjects with ED compared to the general population, with comorbidity ranging from 25 to 75 % (for a review: Godart et al. 2002; Swinbourne and Touyz 2007).

In terms of chronology, anxiety problems have been found to precede ED onset (Deep et al. 1995; Bulik et al. 1997; Godart et al. 2002, 2006; Hildebrandt et al. 2012; Swinbourne et al. 2012) and to predict later development of ED (Kaye et al. 2004; Lilenfeld et al. 2006; Jacobs et al. 2009; Mazzeo and Bulik 2009; Micali et al. 2011). Contributions from longitudinal studies also seem to confirm that child “emotional” characteristics are associated with eating behaviours (Martin et al. 2000; Haycraft et al. 2011) indicating that internalizing characteristics in childhood could predispose to eating disorder later on in life.

Although the co-occurrence of AD and ED has been reported with similar rates for both anorexia nervosa (AN) and bulimia nervosa (BN) by most studies (Godart et al. 2002; Swinbourne and Touyz 2007), some differences have been highlighted.

Whilst obsessive–compulsive disorder and obsessive compulsive personality traits have been found to be highly comorbid in patients with AN, and are predictive of AN (Halmi et al. 1991, 2003, 2005; Rastam et al. 1995; Pollice et al. 1997; Matsunaga et al. 1999; Hoffman et al. 2012), BN patients often present with elevated rates of Post-Traumatic Stress Disorder (PTSD) (Kaye et al. 2004). Hence, while both AN and BN seem to be related to AD, some distinctions seem to exist in relation to specific anxiety disorders or anxiety traits.

## Anxious Personality Traits in Eating Disorders

Cloninger, in his biosocial model of personality, describes four independent temperamental dimensions directly influenced by neurobiological and genetic determinants of behaviours: novelty seeking (reflects behavioural activation and exploration), harm avoidance (represents behavioural inhibition and fearful reaction), reward dependence (assesses behavioural maintenance) and persistence (reflects behavioural perseverance) and three theoretical character traits: self-transcendence, self-directedness (a character dimension subjected to high heritability in twin studies, characterized by low self-esteem and emotional instability), and cooperativeness (Cloninger 1987; Cloninger et al. 1993).

AN and BN have been associated to specific personality traits (Fassino et al. 2002, 2009; Cassin and von Ranson 2005; Lilenfeld et al. 2006; Adambegan et al. 2012): AN has

been consistently associated with low novelty seeking, and high levels of harm avoidance and persistence and low self-directedness; BN has been associated with high novelty seeking and harm avoidance and lower self-directedness.

Accordingly, whilst personality traits of subjects with BN seem to be characterized by impulsivity and emotional dysregulation, those with AN seem to share similar personality traits to those with anxiety disorders, as described by Cloninger et al. (2012) in a recent paper, where high persistence is combined with high harm avoidance, low novelty seeking and low self-directedness.

## Anxiety, Eating Disorders and Parental Characteristics

To better understand the relationship between AD and ED (Lilenfeld et al. 2006) it is useful to research the presence of anxious traits in family members of individuals with ED.

There is evidence that parents of individuals with eating disorders have higher anxiety traits compared to controls (Halmi et al. 1991; Shoebridge and Gowers 2000; Treasure et al. 2001). Accordingly, studies on personality traits consistently found low self-directedness in mothers (Fassino et al. 2002; Monneyron, in preparation), and high harm avoidance in fathers of AN individuals (Fassino et al. 2002, 2009).

Anxious personality traits in parents could for instance be genetically transmitted to the offspring, increasing the liability for both anxiety and ED; but they could also influence parenting style (Hudson and Rapee 2001).

In regards to parenting styles, a recent meta-analysis (Corfield, submitted) showed that individuals with AN and BN tend to describe their parents as overprotective in childhood; but those with BN usually also report lower maternal care compared to controls (Corfield et al., submitted; Fassino et al. 2010). A key study in this area (Shoebridge and Gowers 2000) found that mothers of a sample of 40 adolescent AN patients were significantly more anxious, and retrospectively reported higher levels of overprotection towards their children in childhood than the mothers of the control sample. Accordingly, the majority of mothers reported having provided most of the baby care and having had higher distress when leaving their daughters at nursery. Furthermore, the age when the baby was first left with another adult was higher in the AN group compared to controls. This anxious-overprotective parenting style could be secondary to child fearful temperament, but it is also likely to reinforce child anxiousness or insecurity (Degnan et al. 2010).

Although results from the literature suggest overprotective features in parents of subjects with ED, this has so far only been explored by a small study on adolescents

(Shoebriidge and Gowers 2000). Moreover this study did not investigate offspring temperamental traits.

## The Current Study

The present study aimed (1) to examine early environmental events such as maternal anxiety in pregnancy, and parenting behaviour (overprotection) in siblings discordant for an ED and to investigate differences between AN and BN subgroups; (2) to investigate temperament and childhood separation anxiety in women with AN and BN compared to their unaffected sisters; (3) to determine if any association seen between maternal overprotection and ED could be explained by offspring temperamental traits (novelty seeking, harm avoidance, persistence), indexing “anxious” or “inhibited” personality traits.

We used a discordant sister pair design; this design controls for socio-demographic factors, but more importantly for family environment and values such as attitudes to weight and eating, parental eating problems and family cultural values.

## Methods

### Design

This was a case–control multicenter study (part of a larger European study) using a discordant sister-pair design.

### Sample

Four different European centers took part in the study: the Eating Disorders Research Unit, Institute of Psychiatry, London, UK; the Department of Child Neuropsychiatry, University of Vienna, Austria; the Department of Psychiatry, University Hospital of Bellvitge, Barcelona, Spain, and the Department of Child Psychiatry, University Children's Hospital, Ljubljana, Slovenia.

Cases were mostly recruited and assessed in clinical settings, or through community resources such as websites and volunteer databases from previous research studies (Micali et al. 2007).

Inclusion criteria were: female gender, lifetime diagnosis of AN or BN following DSM IV-TR criteria (APA 2000), presence of a sister close in age, and being a native speaker. The inclusion criteria for the “healthy” sisters were: no eating disturbance [neither AN, BN, nor eating disorder not otherwise specified (EDNOS)] (APA 2000). Moreover, it was required that the age difference between sisters was less than 10 years and the pairs had to have

lived for at least 8 years in the same family, to control for background factors.

Exclusion criteria were: (a) Index cases not meeting diagnostic DSM-IV-TR criteria for AN, BN (APA 2000); (b) age below 16 years; c) current psychotic disorder or learning disability.

The diagnostic algorithm was applied by experienced professionals following a semi-structured clinical interview: the “EATATE” interview (developed for the European Healthy Eating Project; see below). Lifetime diagnosis of AN versus BN was formulated according to the Price Foundation criteria (Kaye et al. 2000), on the basis of a hierarchical model of diagnosis: women with BN irrespective of whether they had a previous history of AN were classified as having BN. This approach is based on the idea that women with BN are phenotypically different from women with AN.

Overall 262 individuals agreed to take part in the study across the four countries. Although 224 women met the study criteria after interview, 21 (9.3 %) were excluded due to the healthy sister being under 16 years of age or meeting criteria for a full or sub-threshold ED. The final sample consisted of 203 women.

Questionnaires about anxiety and overprotection were sent to parents. Of the 203 sister pairs eligible, 157 (77.3 %) parents returned the questionnaires and were included in the study. All 157 sister pairs were asked to complete the TCI-R and were individually interviewed using the ORFI.

### Measures

#### *Eatate Phenotype Interview (Part 1)*

This is a semi-structured interview, comprising an adaptation of the Longitudinal Interval Follow-up Evaluation (LIFE) (Keller et al. 1987) and the Eating Disorders Examination (EDE) (Fairburn and Cooper 1993) developed for the European Healthy Eating Project (QLK-1999-916), which examines genetic and environmental risk factors for eating disorders and obesity (for details see Anderluh et al. 2009). The interview is used to obtain a lifetime history of ED symptoms, which are then plotted on a lifeline. This instrument has been validated and has demonstrated good inter-rater reliability in terms of diagnoses ( $k$  0.82–1.0) and illness history variables (0.80–0.99) (Anderluh et al. 2009). All interviewers were trained in using the interview. Diagnostic validity (compared to clinical notes) yielded  $k$  values between 0.77 and 1.0 for sequential diagnoses. Each sister was interviewed separately. Age, educational level, current body mass index (BMI), and lowest and highest ever BMI at current height were obtained as part of the research interview.

### *Anxiety in Pregnancy and Overprotection*

A self-report questionnaire for mothers about prenatal events was devised by the authors based on the questionnaire used by Shoebridge and Gowers (2000). The same questionnaire also enquired about specific anxiety in pregnancy, general anxiety before the birth of the baby, specific anxiety that the baby would not survive, age (in months) when the child was first left to stay with an adult other than their mother for a few hours, age when the child was first left for an evening in the care of adults other than her main carer, and age when the child was first left for a weekend.

Questions on anxiety in pregnancy had a Likert scale score between 0 and 7 where 0 was “not at all” and 7 was “very much”. For example: “If you could please remember the time you were pregnant with your Child (name): (1) How anxious were you about the pregnancy with your child X; (2) How anxious were you in general (independently from your pregnancy) in the time before the birth of your child X; (3) How anxious were you (while pregnant) that your baby X might not survive?”.

The questionnaire showed good reliability in the present sample (Cronbach Alpha: 0.8).

### *Temperament and Character Inventory-Revised (TCI-R: Cloninger 1999)*

The TCI-R was completed by index women and their healthy sisters. The TCI is a 240 item, reliable, and validated self-report instrument for assessing four temperament (novelty seeking, harm avoidance, reward dependence and persistence) and three character (self-directedness, cooperativeness and self-transcendence) dimensions. Items are rated on a 5-point Likert scale. The TCI has been normed in a large US national probability sample and has shown acceptable internal consistency (Cronbach alpha: 0.76–0.85) (Cloninger et al. 1993; Cloninger 1999).

Temperament traits are heritable (Cloninger et al. 1993) and tend to remain stable during the life course (Cloninger et al. 1993). Cloninger et al. (1993) has also posited that character traits are heritable and influenced by genes.

### *Oxford Risk Factor Interview (ORFI) (Fairburn et al. 1997, 1998)*

The ORFI is a semi-structured interview designed by Fairburn and colleagues to examine the specific risk factors associated with ED. The interview has good inter-rater reliability (Fairburn et al. 1997) with a high level of agreement across the risk factor domains (main weighted kappa: 0.66, SD:  $\pm 0.17$ ) (Fairburn et al. 1997). For the

purpose of this study we focused only on child anxiousness (shyness, separation anxiety). Sisters were interviewed separately by trained interviewers.

### Data Analysis

Data was analysed with SPSS (Version 20 PAWS Statistics) and Stata (Version 11) for Windows. Parametric *t* tests, Analysis of Variance (ANOVA), and non-parametric tests (Wilcoxon, Spearman) were used as appropriate, after testing for normality, to compare continuous variables between ED patients and healthy sisters (allowing for relatedness of the sample).

Correlations were used to investigate whether maternal overprotection was associated to child temperament in index cases.

Conditional logistic regression was used to compare binary and categorical variables across cases and healthy sisters (to account for matching). The significance level used was a two-tailed  $p < 0.05$ .

## Results

### Socio-Demographic Data

Socio-demographic data, divided by country, are shown in Table 1. The majority (99 %) of participants were Caucasian. Regarding women with AN, 37 (39 %) participants were Austrian, 26 (28 %) were English, 17 (18 %) Spanish, and 14 (15 %) Slovenian. For the BN group, 35 (37 %) of the participants were Austrian, 4 (6 %) English, 19 (30 %) were Spanish, and 5 (8 %) Slovenian. As shown in table 1, the affected sisters did not differ significantly on age or educational status from the unaffected sisters. The proband was the eldest sister in 47 % of the cases, and there was no significant difference between index and healthy sisters in terms of order of birth. Mean ages were 25 (SD  $\pm 6.9$ ) for index sisters and 26.1 (SD  $\pm 7.9$ ) for healthy sisters. As expected, the two groups differed on mean BMI at assessment, and lowest and highest BMI at current weight, with the affected sisters revealing significantly lower BMIs in comparison to unaffected sisters. Ninety-four of the affected sisters had a lifetime diagnosis of AN while 63 had a lifetime diagnosis of BN. The age of onset did not significantly differ between the AN and BN groups (respectively mean  $\pm$  SD, years: 17.2  $\pm$  4.4 versus 16.8  $\pm$  3), while duration of illness differed significantly between the two groups (mean  $\pm$  SD, years: AN group = 6.2  $\pm$  5.7 versus BN group = 7.5  $\pm$  4.4,  $p < 0.05$ ). Finally, mean age, education, age of onset, duration of illness and BMI did not vary across the four countries.

**Table 1** Socio-demographic and clinical data: comparison between women with ED and their unaffected sisters

	ED (n = 157)	Unaffected sisters (n = 157)	p values
Mean age ± SD (years)	25.29 ± 6.8	26.1 ± 7.9	NS <sup>1</sup>
Mean BMI at interview	19.39 ± 2.8	22.4 ± 4.2	<0.05 <sup>2</sup>
<i>BMI (median, range) across countries</i>	AN (94)	BN (63)	
England	18.1 (14.6–23.6)	19.9 (17.2–24.2)	
Slovenia	19.4 (15.1–22)	21.6 (14.0–25)	
Austria	18 (13.6–22.8)	19.6 (15.2–22.2)	
Spain	18 (19.1–17.7)	20.1 (18.4–22.5)	
Mean lowest BMI lifetime	14.9 ± 2.7	21.8 ± 3.4	<0.05 <sup>2</sup>
Mean highest BMI lifetime	21.8 ± 3.4	23.6 ± 7	<0.05 <sup>2</sup>
N attended secondary/university education	110 (70 %)	92 (67.7 %)	NS <sup>1</sup>

<sup>1</sup> p values shown were obtained by comparing median values with Mann–Whitney U test

<sup>2</sup> p value obtained by  $\chi^2$  test

**Table 2** Maternal anxiety during pregnancy for AN and BN women and their healthy sisters: median (ranges)

	AN versus healthy sisters (N = 94 pairs)			BN versus healthy sisters (N = 63 pairs)		
	AN (median, range)	Sisters (median, range)	AN versus healthy sisters (N = 94 pairs) Crude OR (95 %CI)	BN (median, range)	Sisters (median, range)	BN versus healthy sisters (N = 63 pairs) Crude OR (95 %CI)
Anxious about the pregnancy	3 (1–7)	2 (1–7)	1.5* (1.0–2.1)	2.5 (1–7)	2 (1–7)	1.0 (0.8–1.5)
Anxious in general before the birth	3 (1–7)	2 (1–7)	1.2 (0.9–1.6)	2 (1–7)	2 (1–7)	1.0 (0.8–1.6)
Anxious that child might not survive after the birth	2 (1–7)	1 (1–7)	1.2(0.9–1.5)	1 (1–6)	1(1–7)	1.0 (0.9–2)
Anxiety during pregnancy (at least one of the above positive)	NA	NA	4* (1.0–14)	NA	NA	1.0 (0.9–2)

OR from conditional logistic regression (outcome: AN versus sister; BN versus sister)

\*  $p \leq 0.05$

<sup>1</sup> Adjusted for novelty seeking, harm avoidance

<sup>2</sup> Adjusted for harm avoidance

### Maternal Anxiety and Overprotection

Table 2 shows results from descriptive statistic for maternal anxiety and results from conditional logistical regression (crude and adjusted OR), using maternal anxiety as a predictor for ED.

In the AN sample we found that mothers reported having experienced higher levels of anxiety (at least one worry) during the pregnancy of the affected child compared to their healthy sister. Higher levels of anxiety (at least one worry) and pregnancy related anxiety, were found to be significantly higher in AN women compared to their healthy sisters.

We also found differences in overprotection in childhood in AN women compared to their healthy sisters. The age in months when the child was left for the first time for a night was significantly higher in index daughters compared to their unaffected sisters. In the BN sub-sample no

differences were found in relation to maternal anxiety and overprotection in childhood between cases and healthy sisters (see Tables 2, 3).

Correlations between temperamental characteristics in women with AN (novelty seeking and harm avoidance) and overprotection variables (age in months when left with another adult; age in months when left for an evening; age in months when left for a weekend) were not significant: for novelty seeking respectively  $r: .46, p = .2$ ;  $r: .07, p = .6$ ;  $r: -.16, p = .3$ ; for harm avoidance respectively  $r: -.02, p = .8$ ;  $r: .07, p = .6$ ;  $r: .19, p = .2$ .

### Childhood Characteristics and Temperament

Childhood characteristics are shown in Table 4. Women in the AN and BN groups were significantly more likely to report separation anxiety in childhood, compared to their. No significant differences were found in relation to shyness.

**Table 3** Overprotection in women with AN and BN and healthy sisters: medians (range) and comparisons from non-parametric tests

Median, range	AN (N = 94)	Sisters (N = 94)	<i>p</i> value <sup>1</sup>	BN (N = 63)	Sisters (N = 63)	<i>p</i> value <sup>1</sup>
Age (months) child was left with someone i.e. grandmother	12 (1.0–96)	12 (1.0–72)	0.1	24 (1.0–69)	24 (1.0–84)	0.7
Age (months) child was left with someone else for the night	12 (1.0–120)	9 (1.0–96)	0.04	12 (3.0–12)	12 (1.0–144)	0.9
Age (months) child was left with someone else for the weekend	27 (1.0–138)	18 (0.5–168)	0.1	36 (12–124)	36 (7.0–144)	0.5

<sup>1</sup> *p* values obtained using Wilcoxon test

**Table 4** Childhood characteristics in AN and BN compared to their healthy sisters: odds ratios (95 % confidence intervals) from conditional logistic regression

	AN (N = 94)	OR (95 % CI)	BN (N = 63)	OR (95 % CI)
<b>Shyness</b>				
Case	25 (30 %)	1.0 (0.7–3.8)	20 (33 %)	1.0 (0.4–2.3)
Healthy sister	16 (20 %)		20 (39 %)	
<b>Separation anxiety</b>				
Case	12 (14.5 %)	9 (1.2–71)**	8 (13.6 %)	6 (1.0–63)*
Healthy sister	2 (2.6 %)		1 (1.6 %)	

\* *p* ≤ 0.05; \*\* *p* < 0.005

Differences in temperament among affected and unaffected sisters are shown in Table 5.

## Discussion

Using a sister-pair design we found that mothers of women with AN reported higher levels of pregnancy-related anxiety while pregnant with AN daughters compared to when pregnant with their healthy daughters. Mothers reported having left their index (AN) daughters with another adult for the first time for an evening at an older age compared to their healthy daughters. This suggests an overprotective attitude towards the daughters with AN in childhood. These findings were specific to AN, as no differences were identified between women with BN and their healthy sisters. Moreover overprotection was not associated with the index daughters' temperament. We also found that daughters with AN were more likely to report separation anxiety problems in childhood compared to their healthy sisters and that they significantly differed from their sisters in terms of anxious traits, i.e. novelty seeking, harm avoidance, persistence, self-directedness.

### Separation Anxiety and Anxious Temperament

In our sample AN patients scored higher on harm avoidance and persistence and lower on novelty seeking and

**Table 5** Temperamental traits and self-directedness in AN And BN compared to their healthy sisters: results from *t* student paired test

	AN sister pairs (N = 94)		BN sister pairs (63)	
	Mean (SD)	<i>p</i>	Mean (SD)	<i>p</i>
<b>Novelty seeking</b>				
Cases	96.6 (16.8)		106.7 (14.4)	
Healthy sisters	109 (12.3)	<0.001	106.4 (13.7)	0.902
<b>Harm avoidance</b>				
Cases	107.5 (22.5)		108.1 (17.1)	
Healthy sisters	96.6 (15.3)	<0.001	97.4 (15.3)	0.001
<b>Reward dependence</b>				
Cases	102.8 (11.5)		106.1 (17.07)	
Healthy sisters	108.3 (11.5)	0.005	104.1 (8.6)	0.393
<b>Persistence</b>				
Cases	120.2 (17.7)		112.2 (15.5)	
Healthy sisters	108.7 (20.8)	<0.001	110.3 (15.8)	0.471
<b>Self-directedness</b>				
Cases	128 (22.4)		125.4 (22.3)	
Healthy sisters	141.9 (18.4)	<0.001	139.9 (14.8)	<0.001

self-directedness compared to their sisters, supporting findings from previous studies on the association between AN and anxious personality traits (Karwautz et al. 2002; Lilienfeld et al. 2006; Amianto et al. 2011). This personality profile seems to resemble the one described by Cloninger et al. (2012) in relation to individuals with anxiety disorders. In contrast women with BN were found to score higher on harm avoidance and lower on self-directedness, but had similar levels of novelty seeking and persistence, compared to their healthy sisters. These results support an “insecure-fearful-anxious” personality style in women with AN (but not in BN), likely to be present since early childhood. Supporting this assumption, in our sample separation anxiety in childhood was found to be highly associated with both ED subtypes (AN and BN), with higher scores being characteristic especially of AN individuals. This also confirms previous findings on the association between separation anxiety and AN (Shoebridge and Gowers 2000; Silberg and Bulik 2005; Troisi et al. 2006)



and indicates the presence of a fearful, anxiety-prone, early childhood profile in AN women.

### Maternal Anxiety and Overprotection

Our findings revealed that pregnancy-related anxiety during the index pregnancy was associated with AN. Many studies have shown that antenatal maternal anxiety and/or stress produces Hypothalamus–Pituitary–Adrenal axis (HPA) hyperactivation in offspring, which in turn has been found to: increase susceptibility to anxiety and depression; predict childhood behavioural and emotional problems; and produce long lasting effects in terms of cognitive and behavioural development (Blair et al. 2011; Glover and Hill 2012; Micali et al. 2011; O'Connor et al. 2002; Van den Bergh et al. 2005; Talge et al. 2007). Recent research has found evidence for a specific association between pregnancy-related anxiety and emotional and cognitive development of infants (Blair et al. 2011).

Regarding overprotection we also found, in accordance with Shoebridge and Gowers' findings (2000), that the age when the index child was first left with another adult overnight was significantly higher in sisters with AN compared to their healthy sibling, possibly indicating an overprotective attitude towards the child who later developed AN. However overprotection was not correlated to the daughters' temperament traits and was not influenced by birth order, as there was no difference in first-born women amongst index siblings.

A possible explanation for maternal overprotection has been speculated in relation to perinatal (such as pregnancy/obstetric complications) or stressful events occurring in pregnancy (i.e. loss of a member of the family): these events could increase maternal anxiety during the index pregnancy and might lead to later maternal overprotection towards the index child, as previously suggested (Shoebridge and Gowers 2000).

Interestingly our finding was specific to women with AN, and no differences were found between women with BN and their healthy sisters. It is worth noting that this null finding could be due to low power to detect differences in the BN group.

In relation to risk mechanisms it is interesting that a recent study (Amianto et al. 2011), investigating a sample of non-twin sisters (discordant for AN), found that both sisters reported significantly higher levels of parental overprotection, compared to controls; however in the study only sisters with AN within the sister-pairs were displaying an insecure attachment. There is initial evidence to support a gene–environment interaction model, where some individuals are more sensitive to certain parenting styles (than, for example, their siblings) and this sensitivity impinges on the risk of ED (Karwautz et al. 2011).

A possible explanation for our findings is that genetic and/or neurobiological vulnerability (i.e. exposure to high maternal stress in utero, temperamental traits) could condition a particular response to environmental stimuli (i.e. sensitivity to separation) and increase the risk for AN.

### Strengths and Limitations

Our findings have to be interpreted in the context of relevant strengths and limitations. This study used a sister-pair design, which controls for many familial, cultural and environmental factors. Moreover this study relies on a large sample of clinically defined cases, assessed by skilled clinicians and researchers using a standardized tool.

Although the study relied on a large sample of European participants, 99 % of the participants were Caucasian, and therefore results are only generalizable to Caucasian populations. Another limitation is that the data on self-reported maternal anxiety in relation to the index offspring could be subject to “searching for meaning”. However, our findings that the association found between overprotection and ED was specific to AN and not to BN, and the fact that our data replicate previous findings point to a true association. Separation anxiety was reported retrospectively by participants and therefore is subject to recall bias. Finally, we measured temperament in adults with the underlying assumption that temperament traits are stable throughout life (Caspi et al. 2005) and have a strong genetic influence (Cloninger et al. 1993); however changes can occur and original traits can be modified by life events/experiences.

### Conclusions

A significant association between adult AN and maternal anxiety in pregnancy and overprotection in childhood was identified. AN patients displayed more anxious characteristics in childhood and anxious temperament traits, compared to their healthy sisters. However the effect of maternal overprotection on offspring AN was not explained by their child anxious temperament. This was not the case for women with BN where both maternal anxiety and overprotection were similar between index and healthy sisters. This finding lends speculation to the risk for AN being linked to maternal stress and anxiety in utero and later on to overprotective care. An alternative explanation is that our findings are underpinned by a shared genetic liability between anxiety and AN. Our findings have important implications for our understanding of risk factors for ED that might contribute to better prevention of the disorders in the future. Future larger studies should employ a longitudinal design to investigate the specific effects of maternal anxiety on AN.

**Acknowledgments** This study was supported by the European Commission Framework V programme (QLK1-1999-916), a grant from the PPP foundation (1206/87) to J.L.T. and D.C., and partially by FIS (G3/184). Dr. Krug was supported by a Marie-Curie Intra European Fellowship within the 7th European Community Framework Programme, as No. 254774 (call reference: FP7-PEOPLE-2009-IEF). Financial support was received from Fondo de Investigación Sanitaria (PI11/210) and AGAUR (2009SGR1554). CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn) is an initiative of ISCIII.

**Conflict of interest** None.

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