RESEARCH ARTICLE

Social and Emotional Processing as a Behavioural Endophenotype in Eating Disorders: A Pilot Investigation in Twins

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Abstract

Objectives: Emotional processing difficulties are potential risk markers for eating disorders that are also present after recovery. The aim of this study was to examine these traits in twins with eating disorders.

Methods: The Reading the Mind in the Eyes test, Emotional Stroop task and the Difficulties in Emotion Regulation Scale were administered to 112 twins with and without eating disorders (DSM IV-TR eating disorder criteria). Generalised estimating equations compared twins with eating disorders against unaffected co-twins and control twins, and within-pair correlations were calculated for clinical monozygotic ($n = 50$) and dizygotic twins ($n = 20$).

Results: Emotion recognition difficulties, attentional biases to social threat and difficulties in emotion regulation were greater in twins with eating disorders, and some were present in their unaffected twin siblings. Evidence for a possible genetic basis was highest for emotion recognition and attentional biases to social stimuli.

Conclusion: Emotion recognition difficulties and sensitivity to social threat appear to be endophenotypes associated with eating disorders. However, the limited statistical power means that these findings are tentative and require further replication. Copyright © 2013 John Wiley & Sons, Ltd and Eating Disorders Association.

Keywords

endophenotype; eating disorder; emotion; heritable; familial

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Introduction

Symptoms in the acute state of eating disorders can be confounded by malnutrition and disrupted eating behaviours (Kaye, Fudge, & Paulus, 2009; Brockmeyer et al., 2012; Treasure, Corfield, & Cardi, 2012). This makes it difficult to distinguish between clinical symptoms that are secondary to state alterations and those that are primary bio-psychological risk factors. A solution has been to investigate endophenotypes, which are measurable, heritable factors that exist on the pathway between the genotype and the phenotype (Gottesman & Gould, 2003). Endophenotypes have the potential to assist in informing a more biologically based taxonomy of psychiatric disorders (Bulik et al., 2007) and become targets in future treatments. Previously, there has been evidence to suggest that cognitive styles are endophenotypes of eating disorders (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005; Roberts, Tchanturia, & Treasure, 2010; Tenconi et al., 2010; Kanakam, Raoult, Collier, & Treasure, 2012). However, it remains unclear as to whether the social emotional difficulties that characterise people with eating disorders are primary or secondary illness factors.

Emotional processing difficulties in relation to eating disorder symptoms

Emotional, social communicative and interpersonal difficulties are of empirical importance because they are predictive of the long-term clinical outcome in people with eating disorders (Zipfel, Löwe, Reas, Deter, & Herzog, 2000; Herpertz-Dahlmann et al., 2001; Wentz, Gillberg, Anckarsäter, Gillberg, & Råstam, 2009; Schulte-Rüther, Mainz, Fink, Herpetz-Dahlmann, & Konrad, 2012). Some aetiological models of eating disorders propose that this emotional profile exists premorbidly, as a consequence of genetic factors, and can be modified by environmental factors such as birth complications, adverse perinatal events, attachment styles and interpersonal events (Kaye, 2008; Treasure et al., 2012). These include genetically driven variation in 5-HTT function, which can lead to hyper-responsiveness of the amygdala and sensitivity to emotional stimuli (Hariri et al., 2002). Emotional processing difficulties are amplified in the acute state, and disordered eating behaviour is often used as a maladaptive strategy to regulate emotion (Haynos & Fruzzetti, 2011). These include emotional avoidance and suppression strategies (Aldao, Nolen-Hoeksema, & Schweizer, 2010) such as binge eating (Heatherton

& Baumeister, 1991) and caloric restriction. The latter leads to a reduction in the availability of synaptic 5-HT (Kaye et al., 2009; Frank & Kaye, 2012). Both of these strategies are positively reinforced as they lead to a temporary reduction in anxiety and, in some cases, the start of a vicious cycle (Kaye, 2008).

Difficulties in complex emotion recognition

It is unclear whether all aspects of the emotional processing profile are transdiagnostic features. A review of emotional processing in people with eating disorders (Oldershaw et al., 2011) concluded that women with anorexia nervosa have difficulties in their ability to infer emotional states in others. There is conflicting evidence in bulimia nervosa, with two studies demonstrating difficulties (Harrison, Sullivan, Tchanturia and Treasure, 2010; Medina-Pradas, Blas Navarro, Alvarez-Moya, Grau, & Obiols, 2012) and one study of women with a diagnostic mix of bulimia nervosa not demonstrating any significant difficulties on the Reading the Mind in the Eyes test (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001) or in a more complex task of emotional recognition in films (Kenyon et al., 2012). After recovery from anorexia nervosa, difficulties on the Reading the Mind in the Eyes test remain in an attenuated form (Harrison, Tchanturia and Treasure, 2010), whereas performance on the more complex task of emotional recognition in films is restored to normal levels (Oldershaw et al., 2011). Supporting a possible biological basis to this feature, functional magnetic resonance imaging studies have shown reduced activation in the right temporoparietal junction in those who have recovered from anorexia nervosa when completing a theory of mind task (McAdams & Krawczyk, 2011). Other studies of patients with anorexia nervosa who are weight recovered have shown reduced activation in the middle and anterior temporal cortex and in the medial prefrontal cortex when completing a theory of mind task (Schulte-Rüther et al., 2012). This hypoactivation of the medial prefrontal cortex is associated with clinical outcome at a 1-year follow up. As of now, there are no studies of genetically informative samples to indicate whether this may be an endophenotype of eating disorders. However, there is evidence from other psychiatric disorders such as autistic spectrum disorder (Baron-Cohen & Hammer, 1997; Losh & Piven, 2007) and schizophrenia (de Achával et al., 2010; Ibanez, Manes, Cetkovich, Hurtado, & Reyes, 2010) to suggest that emotional recognition difficulties, measured by the Reading the Mind in the Eyes test, may be a familial trait.

Attentional biases to social stimuli

Social attentional biases are argued to arise from an increase in activity in the amygdala, which lowers activation in the sensory systems, thereby increasing attentional vigilance to emotional stimuli (Davis & Whalen, 2001). This increase in activity has been linked to those carrying the short allelic form of the 5-HTTLPR (Pergamin-Hight, Bakermans-Kranenburg, van Ijzendoorn, & Bar-Haim, 2012). A review of studies (Oldershaw et al., 2011) has concluded that overall, people with anorexia nervosa selectively attend to social emotional information, particularly to anger on the Emotional Stroop task (Ashwin, Wheelwright, & Baron-Cohen, 2006). There is also evidence of this feature in women with bulimia nervosa (Harrison et al., 2010). A different measure, the dot-probe task (Dandeneau & Baldwin, 2004), found an attentional bias to faces expressing rejection and attentional avoidance of accepting faces to be transdiagnostic features (Cardi, Matteo, Corfield, & Treasure, 2012). Evidence of these features remaining after recovery in women with anorexia nervosa (Harrison, Tchanturia and Treasure, 2010; Cardi et al., 2012) and bulimia nervosa (Cardi et al., 2012) indicates that they may be premorbid traits. The genetic basis of these specific features has not yet been investigated in people with eating disorders. However, there may be a biological basis to emotional vigilance, which is evident from the differential brain activation that occurs when classifying emotion (Kühnpast, Pollatos, & Schandry, 2009) and when responding to happy and neutral faces (Hassel et al., 2009). In women with bulimia nervosa, there is a decreased neural response in the precuneus and the right amygdala to facial expressions of disgust and anger (Ashworth et al., 2011). On the other hand, a smaller study of women who have recovered from anorexia nervosa found no difference in neural responses to happy and sad faces (Cowdrey, Harmer, Park, & McCabe, 2012). From the evidence base, it may be concluded that anomalies in attentional processes to emotional stimuli are a transdiagnostic feature, which may persist after recovery. Even so, the evidence appears to be stronger for anorexia nervosa, possibly because of the limited number of studies of people with bulimia nervosa (DeJong et al., 2011).

Difficulties in emotion regulation

Women with eating disorders (anorexia nervosa and bulimia nervosa) display difficulties in emotional regulation [measured by the Difficulties in Emotion Regulation self-report questionnaire (Gratz & Roemer, 2008)] (Harrison, Sullivan, Tchanturia, & Treasure, 2009; Harrison, Sullivan, et al., 2010; Harrison, Tchanturia and Treasure, 2010). This denotes an inability to behave in such a way that accounts for long-term goals when emotional arousal is of great intensity (Fruzzetti, Crook, Erikson, Lee, & Worrall, 2008). These difficulties may be suggestive of a biological vulnerability because they have been found to persist in an attenuated form in women who have recovered from anorexia nervosa (Harrison, Tchanturia and Treasure, 2010). Due to a lack of evidence, it is unclear whether this trait persists in people who have recovered from bulimia nervosa.

The current study

The methodology, which has been adopted in the aforementioned studies, does not distinguish whether emotional processing difficulties are a genetic risk or a consequence of the illness. Therefore, the current study investigated a twin sample that provided a natural experiment to parse out the effects of genetic and environmental influences (Plomin, De Fries, McClearn, & McGuffin, 2001). Three criteria used to define endophenotypes as outlined by Gottesman and Gould (2003p. 639) were investigated: (1) the trait's 'association with the illness in the population' was examined by comparing eating disorder twins with control twins, (2) the trait's 'co-segregation with the illness in families' was assessed by comparing unaffected co-twins with controls twins and (3) the trait's 'heritability' was explored by comparing clinical monozygotic and dizygotic twins with the expectation that performance within monozygotic twin pairs will be more similar because they share 100% of genes, in comparison with dizygotic twin pairs who share on average only 50% of genes. It is noted that the

proportion of shared genes is an approximation because epigenetic effects can contribute to genetic differences within monozygotic and dizygotic twin pairs (Singh, Murphy, & O'Reilly, 2002; Bruder et al., 2008).

Method

Ascertainment and recruitment

A total of 82 (73.2%) female twins with and without eating disorders were recruited from the St. Thomas UK twin registry (www.twinsuk.ac.uk) (composed of 12,000 twins representative of the general population), who responded to a newsletter advertising the study. Additional twins were recruited from a previous study conducted by Holland, Sicotte, and Treasure (1988) ($n = 14$, 12.5%). The remainder of the twins ($n = 16$, 14.3%) were recruited through advertisements posted on the departmental website for the Eating Disorder Research Unit at King's College London. The twins were ascertained on the basis of clinical status and zygosity.

Participants

In total, 112 twins (56 female twin pairs) participated, aged 16 to 60 years. Self-defined ethnicity indicated that the majority (91%) were White British. English was the first language for all but one set of twins from the clinical group. Zygosity was determined by a DNA test for 73.2% of the twins. The remaining cases (26.8%) were administered the 'peas in a pod' questionnaire (96–98% accurate) to determine zygosity as advised by the UK Twin Registry (Peeters, Van Gestel, Vlietinck, Derom, & Derom, 1998).

Twins with eating disorders and their unaffected co-twins group

This group consisted of 51 twins who had a diagnosis of an eating disorder and 19 of their unaffected co-twins. This included 16 concordant pairs (14 monozygotic and 2 dizygotic pairs) and 19 discordant pairs (11 monozygotic and 8 dizygotic pairs). The probandwise concordance rate for lifetime eating disorders was 72% in monozygotic twins and 33% in dizygotic twins. The twins reported cohabiting with one another for a mean duration of 20.8 years (range: 15–45 years).

Twins with eating disorders were separated by diagnosis into two broad groups: (1) 'bulimic disorder' [composed of bulimia nervosa, eating disorder not otherwise specified-bulimia nervosa and binge eating disorder as proposed by Van den Eynde et al. (2011)] and (2) 'anorexia nervosa' (including anorexia nervosa, anorexia nervosa-binge/purge subtype and eating disorder not otherwise specified-anorexia nervosa) (DSM-IV TR; American Psychiatric Association, 2000). One monozygotic twin with eating disorder not otherwise specified-inappropriate compensatory behaviours was excluded from this grouping. For the twins with eating disorders, 52.9% ($n = 27$) began with an episode of restricted eating (anorexia nervosa), and 72.5% ($n = 37$) experienced a loss of control over eating (binge eating) during their lifetime. For our twins with eating disorders, 62.8% ($n = 32$) reported recovery, defined as no reporting of behavioural or psychological symptoms associated with eating disorders for 2 years or more (Uher et al., 2003). In total, only 39.2% ($n = 20$) had received treatment.

Control twin group

The control group included 42 twins (composed of 17 monozygotic and 4 dizygotic twin pairs). The twins reported cohabiting together for a mean duration of 21.4 years (range: 18–30 years).

Exclusion and inclusion criteria for the clinical and control samples

Twins were excluded if they had a visual impairment without a corrective aid, a neurological condition, a head injury, current epilepsy or an IQ below 70 [measured by the National Adult Reading Test (Nelson & Willison, 1991); see General Assessment section].

(i) Exclusion and inclusion criteria for twins with eating disorders and their co-twins

Clinical twins were included if they had a primary diagnosis of a lifetime eating disorder (DSM IV-TR criteria, 2000) or a history of eating disorder not otherwise specified-inappropriate compensatory behaviours and if their co-twin (unaffected or also with an eating disorder) was able to participate. Due to the difficulties in recruiting twins with eating disorders, the present study included eating disorder twins in many different phases of the illness, such as those who were not underweight [body mass index (BMI) 18.5] or currently recovered. In line with current diagnostic approaches, amenorrhoea was not required for a diagnosis of anorexia nervosa (Thomas et al., 2010).

(ii) Exclusion and inclusion criteria for control twins

Control twin pairs were included if both had a healthy BMI between 19 and 25 kg/m^2 and they had no personal or family history of an eating disorder or other psychiatric diagnosis. They were excluded if they scored above the cut-off on one or more self-report measure that screened for the presence of disordered eating behaviour [Eating Disorder Diagnostic Scale (Stice, Telch, & Rizvi, 2000)], the presence of obsessive compulsive behaviour [Obsessive Compulsive Inventory-Revised, (Foa et al., 2002)] as well as depression (20>), anxiety (14>) or stress (25>) [Depression Anxiety and Stress Scale (Lovibond & Lovibond, 1995)].

Clinical assessment

All eating disorder twins and non-eating disorder co-twins were interviewed with the EATATE lifetime diagnostic interview (Anderluh, Tchanturia, Rabe-Hesketh, & Treasure, 2003) to obtain a lifetime history of eating disorder symptoms. It was administered by a trained doctoral researcher, and diagnosis was confirmed by a clinician. This semi-structured interview is composed of a European adaptation of the Longitudinal Interval Follow-up Evaluation (Keller et al., 1987) and the Eating Disorders Examination questionnaire (Fairburn & Cooper, 1993). It has been used previously in research of women with anorexia nervosa (Anderluh, Tchanturia, Rabe-Hesketh, Collier, & Treasure, 2009) and demonstrates good inter-rater reliability in terms of diagnoses (kappa 0.82–1.0) and illness history variables (0.80–0.99).

Emotional processing assessment

The Reading the Mind in the Eyes test (Baron-Cohen et al., 2001) is a validated assessment of emotion recognition. The participant is presented with 36 slides containing sets of eyes. This includes 17 women and 19 men, depicting the face from the brow down to the nose, midway. The participant is required to choose one word out of four that most closely resembles what the person is thinking or feeling. A definition handbook is provided. The outcome measure is the percentage of correct answers, and a lower score indicates greater difficulties in emotion recognition.

The Emotional Stroop (Ashwin et al., 2006) is a computerised task that measures response times to social stimuli. This includes attentional bias towards (1) social stimuli (female and male, neutral and angry faces), (2) social threat stimuli (female and male, angry faces) and (3) non-social stimuli (pictures of a chair). The stimuli are tinted red, yellow, blue or green and are presented in a random order, in three blocks of 48, with two breaks to rest.

Each stimulus ($n = 144$) is presented for a maximum of 4000 milliseconds. Individuals are instructed to name the colour of the picture they see as quickly as possible. A practice trial ensures that the instructions are understood and that their voice is detected. Response times are recorded using the DMDX software (Forster & Forster, 2003).

The outcome scores are the social attentional bias and social threat attentional bias variables. The social attentional bias variable is derived by subtracting the mean time to colour-name non-social stimuli from the mean time to colour-name all of the social stimuli. Positive scores indicate longer response latencies for social stimuli, and negative scores indicate longer response latencies for non-social stimuli.

The social threat attentional bias variable is derived by subtracting the mean response time to colour-name social neutral stimuli from the mean response time to colour-name social threat stimuli. Positive scores indicate longer response latencies for social threat stimuli, and negative bias scores indicate longer response latencies for social neutral stimuli.

The Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004) is a 36-item self-report measure. Participants are required to indicate how often each statement applies to them, ranging from 1 (0–10% of the time) to 5 (91–100% of the time). The outcome score is the sum of all the items, and higher scores indicate greater difficulties in emotion regulation.

General assessment

The National Adult Reading Test (Nelson & Willison, 1991) provides an indication of premorbid IQ. Participants are required to read aloud a list of words. A greater number of incorrect pronunciations indicates a lower premorbid IQ. The outcome score correlates positively with overall performance on the British version of the Wechsler Adult Intelligence Scale (Crawford & Parker, 1989; Crawford et al., 1992).

The Depression Anxiety and Stress Scale (Lovibond & Lovibond, 1995) is a 21-item self-report measure assessing levels of depression, anxiety and stress (Cronbach's Alpha = 0.86 for total score).

Procedure

Information and consent forms were sent prior to the appointment. The Reading the Mind in the Eyes test was administered before the Emotional Stroop task (following the methodology of Harrison, Sullivan, et al., 2010; Harrison, Tchanturia and Treasure, 2010). Self-report questionnaires (which included the Difficulties in Emotion Regulation Scale) were completed before the Reading the Mind in the Eyes test and the Emotional Stroop task, and the diagnostic interviews were completed afterwards. It was emphasised that involvement in the study was voluntary and they were free to withdraw at anytime. This study was approved by the South London and Maudsley NHS Trust Research Ethics Committee.

Statistical methods

For the familial analysis, differences between 'eating disorder probands' (monozygotic and dizygotic probands; Table I), 'non-eating disorder co-twins' (monozygotic and dizygotic non-eating disorder co-twins; Table I) and control twins (monozygotic and dizygotic control twins) were analysed using the generalised estimating equation model for non-independent data (Liang & Zeger, 1986). This accounts for the correlative nature of twin pairs (i.e. controls for zygosity). The Depression, Anxiety and Stress measure (Lovibond & Lovibond, 1995) was included as a covariate because this feature differed significantly between groups.

To compare diagnostic differences, non-eating disorder co-twins were separated on the basis of their probands diagnosis into the non-anorexia nervosa co-twins and non-bulimic disorder co-twin groups. Because of the limited sample size for eating disorder not otherwise specified-inappropriate compensatory behaviours ($n = 1$), this twin and her non-eating disorder co-twin were excluded from this analysis (Table III).

Cohen's d effect sizes were calculated for each comparison with an effect size calculator, using descriptive statistics that were based on the Depression Anxiety and Stress Scale covariate (Lovibond & Lovibond, 1995). Differences are defined as negligible (≥ 0.0 and < 0.15), small (≥ 0.15 and < 0.40), moderate (≥ 0.40 and < 0.75), large (≥ 0.75 and < 1.10), very large (≥ 1.10 and < 1.45) and huge (≥ 1.45).

Within-pair correlations were calculated separately for monozygotic and dizygotic twins with eating disorders and their unaffected co-twins. These intraclass correlation coefficients analyse how strongly twin 1 resembles twin 2. This analysis was not carried out for the control twin group because the dizygotic twin sample size was too small ($n = 8$).

This study was exploratory, because it was the first time the Emotional Stroop task (Ashwin et al., 2006), the Reading the Mind in the Eyes test (Baron-Cohen et al., 2001) and the Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004) were administered to twins with eating disorders. To reduce the risk of a type I statistical error, an alpha level of 0.05 was used to report significant results. Sufficient statistical power was not always attained because of the limited twin sample size. Therefore, it was decided to report group differences that occurred at 'trend level' and attained a reasonable effect size (i.e. Cohen's d greater than 1) but did not reach statistical significance. Highlighting trends that are in line with previous research explores whether the findings from this twin sample can be generalised to the

Table 1 Demographic and clinical features for twins with a lifetime eating disorder diagnosis and their non-eating disorder co-twins separated by zygosity (monozygotic and dizygotic) and controls twins

	MZ-ED (39)	MZ-non-ED (11)	DZ-ED (12)	DZ-non-ED (8)	Control Twins (42)	Test statistic
Age	38.28 (14.45)	46.64 (16.84)	39.17 (14.64)	42.88 (16.85)	42.57 (12.82)	Wald Chi Square: 7.3, $df = 4$, $p = 0.12$
BMI current	21.60 (5.53)	22.28 (3.94)	21.16 (1.22)	22.70 (2.55)	22.51 (2.60)	Wald Chi Square: 11.2, $df = 4$, $p = 0.02$
BMI lowest	16.99 (4.91)	19.48 (2.00)	16.88 (1.86)	18.80 (3.00)	–	Wald Chi Square: 15.8, $df = 3$, $p = 0.00$
BMI highest	23.81 (4.6)	23.15 (6.1)	23.89 (3.7)	24.16 (6.3)	–	Wald Chi Square: 0.3, $df = 3$, $p = 0.97$
Age of onset	17.46 (4.19)	–	19.92 (6.50)	–	–	–
Duration of illness (in years)	11.56 (11.44)	–	8.17 (10.45)	–	–	–
IQ estimated by the National Adult Reading Test (Range: 18 to 126)	108.10 (8.98)	110.80 (8.70)	106.25 (10.42)	110.88 (7.74)	110.22 (7.15)	Wald Chi Square: 3.8, $df = 4$, $p = 0.43$
Depression Anxiety and Stress Scale (Range: 0 to 100)	39.24 (31.25)	18.73 (17.40)	34.73 (33.90)	25.14 (16.73)	14.71 (11.26)	Wald Chi Square: 25.0, $df = 4$, $p = 0.00$
Lifetime eating disorder diagnosis	Anorexia nervosa = 46.2%: (anorexia nervosa-restricting: $n = 10$, anorexia nervosa-binge/purge: $n = 8$) Bulimic disorder = 51.3%: (bulimia nervosa: $n = 16$, eating disorder not otherwise specified-bulimia nervosa: $n = 2$, binge eating disorder: $n = 2$) Inappropriate compensatory behaviours = 2.6% (n = 1)	–	Anorexia nervosa = 50%: (anorexia nervosa-restricting: $n = 2$; anorexia nervosa-binge/purge: $n = 1$, eating disorder not otherwise specified-anorexia nervosa: $n = 3$) Bulimic disorder = 50%: (bulimia nervosa = 6)	–	–	–
Recovered	56.4%	–	83.3%	–	–	–
BMI > 18.5	84.6 %	–	100%	–	–	–
Years of recovery	10.03 (13.45) (Range: 0–41)	–	11.08 (12.34) (Range: 0–41)	–	–	–

Note:
Twins are separated on the basis of zygosity and clinical status.
Means and standard deviation in brackets (two decimal places).
MZ-ED, monozygotic eating disorder twins; MZ-non-ED, monozygotic non-eating disorder cotwins; DZ-ED, dizygotic eating disorder twins; DZ-non-ED, dizygotic non-eating disorder cotwins; BMI, body mass index.

singleton population with eating disorders. Many psychiatric conditions are thought to develop as a consequence of a combination of risk traits, each with small effects (Gottesman & Gould, 2003), therefore making it necessary to report these.

Spearman's Rho correlation coefficients assessed associations between behavioural task performance and clinical features in twins with eating disorders. The duration of clinical symptoms was weighted by age. In line with the argument of Rothman (1990), a correction for multiple testing was not required because the outcome variables were related. All analyses were carried out using PASW Statistics version 18.

Sample size and power

The sample size in the present study was limited by the number of twins with eating disorders it was possible to recruit. Because of the exploratory nature of this study, a *post hoc* power analysis was conducted using G-Power software. This indicated that the present sample would have 66%, 97%, 100% and 100% power for detecting group differences between eating disorder twins and controls at the 0.05 level for the Reading the Mind in the Eyes test, Emotional Stroop task social attentional bias and social threat attentional bias and the Difficulties in Emotion Regulation Scale respectively (based on Harrison et al., 2009; Harrison, Sullivan, et al., 2010; Harrison, Tchanturia and Treasure, 2010).

Results

In Table I, the twins with eating disorders, non-eating disorder co-twins (i.e. unaffected co-twins) and controls were separated on the basis of zygosity and clinical status. There were no significant differences between the groups for age (Wald Chi Square: 7.3, $df = 4$, $p = 0.12$) or IQ (estimated by the National Adult Reading Test: Nelson & Willison, 1991) (Wald Chi Square: 3.8, $df = 4$, $p = 0.43$). However, the groups were significantly different for BMI (Wald Chi Square: 11.2, $df = 4$, $p = 0.02$) and levels of depression, anxiety and stress [Wald Chi Square: 25.0, $df = 4$, $p = 0.00$ (measured by the Depression Anxiety and Stress Scale; Lovibond & Lovibond, 1995)].

Analysis of emotional processing difficulties as familial traits

The following analysis explores two endophenotype criteria as outlined by Gottesman and Gould (2003): (1) the trait should be associated with the illness, and (2) the trait should co-segregate with the illness in families. Tables II and III and Figures 1–6 present the results for comparing eating disorder twins, non-eating disorder co-twins and controls on emotional processing measures.

(i) Eating disorder twins vs. control twins

Table 2 Analysis of emotional processing in eating disorders and as a familial trait

Analysis for 'overall groups': ED twins, non-ED co-twins and controls						
	ED twins	Non-ED co-twins	Control twins			
	($n = 51$)	($n = 19$)	($n = 42$)	Group comparisons, mean difference (95% CI) p value		Cohen's d
Reading the Mind in the Eyes test (% correct)† (Range: 47.1 to 94.2%)	74.94 (3.75)	75.31 (2.96)	76.19 (3.36)	Wald Chi Square: 0.31, $df = 2$, $p = 0.86$		
				ED twins < control twins , −1.25 (5.78–3.29)	$p = 0.59$	($d = -0.1$)
				Non-ED cotwin < control twins, 0.88 (−5.26 to 3.50)	$p = 0.69$	($d = -0.1$)
Emotional Stroop task social attentional bias (in ms)† (Range: −75.9 to 185.9)	17.66 (45.40)	9.17 (28.96)	6.79 (27.03)	Wald Chi Square: 0.72, $df = 2$, $p = 0.70$		
				ED twins > control twins, 10.87 (−14.30 to 36.04)	$p = 0.40$	($d = 0.3$)
				Non-ED cotwin > control twins −2.37 (−12.15 to 16.89)	$p = 0.75$	($d = 0.1$)
Emotional Stroop task social threat attentional bias (in ms)† (Range: −98.7 to 85.8)	8.24 (32.90)	−12.52 (39.52)	−7.39 (21.68)	Wald Chi Square: 0.63, $df = 2$, $p = 0.04$		
				ED twins > control twins, 15.63 (2.29–28.97)	$p = 0.02$*	($d = 0.6$)
				Non-ED cotwin < control twins, −5.13 (−22.23 to 11.96)	$p = 0.56$	($d = -0.2$)
Difficulties in Emotion Regulation† (Range: 39 to 153)	86.58 (29.97)	85.63 (24.47)	76.223 (16.72)	Wald Chi Square: 6.89, $df = 2$, $p = 0.03$		
				ED twins > control twins, 10.35 (1.56–19.14)	$p = 0.02$*	($d = 0.4$)
				Non ED co-twin > control twins, 9.34 (−2.11 to 20.90)	$p = 0.11$	($d = 0.5$)

Note:
ED twins, monozygotic twins and dizygotic twins with eating disorders; non-ED co-twins, monozygotic and dizygotic non-eating disorder co-twins; controls twins, monozygotic and dizygotic twins.
Descriptive statistics presented are raw means and standard deviations (two decimal places)
†Data were analysed with the Depression Anxiety and Stress Scale (Lovibond & Lovibond, 1995) included as a covariate, Reading the Mind in the Eyes test (Baron-Cohen et al., 2001), Emotional stroop task (Ashwin et al., 2006), and Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004).
*$p < 0.05$

Table 3 Analysis of emotional processing for 'overall groups' sub-divided by eating disorder diagnosis and as a familial trait

Analysis for 'overall groups' sub-divided by eating disorder diagnosis								
Specific diagnosis (NB)	AN twins ($n=24$)	BD twins ($n=26$)	Non-AN co-twins ($n=12$)	Non-BD co-twins ($n=6$)	Control twins ($n=42$)	Group comparisons, mean difference (95% CI) p Value		Cohen's d
Reading the Mind in the Eyes test (% correct)†	73.13 (10.15)	76.52 (10.65)	75.42 (8.36)	75.18 (8.53)	76.22 (9.24)	Wald Chi Square: 2.86, $df=4$, $p=0.58$		
						AN twins < control twins, −2.93 (−7.72 to 1.86)	$p=0.23$	($d=-0.3$)
						BD twins = control twins, 0.05 (−4.71 to 4.81)	$p=0.98$	($d=-0.0$)
(Range: 47.1 to 94.2%)						Non-AN co-twins < control twins, −1.14 (−7.03 to 4.74)	$p=0.70$	($d=-0.1$)
						Non-BD co-twins < control twins, −2.47 (−7.74 to 2.80)	$p=0.36$	($d=-0.2$)
Emotional Stroop task social attentional bias (in ms)†	11.25 (35.66)	23.14 (53.22)	13.54 (32.71)	2.53 (22.65)	7.06 (27.63)	Wald Chi Square: 3.05, $df=4$, $p=0.55$		
(Range: −75.9 to 185.9)						AN twins > control twins, 2.87 (−13.19 to 18.92)	$p=0.69$	($d=0.1$)
						BD twins > control twins, 14.96 (−11.24 to 41.16)	$p=0.35$	($d=0.4$)
						Non-AN co-twins > control twins, 0.29 (−17.02 to 17.60)	$p=0.49$	($d=0.2$)
						Non-BD co-twins < control twins, −7.81 (−25.51 to 9.89)	$p=0.63$	($d=-0.2$)
Emotional Stroop task social threat attentional bias (in ms)†	3.65 (26.65)	12.98 (37.80)	−28.59 (38.48)	12.44 (21.70)	−7.72 (21.68)	Wald Chi Square: 17.5, $df=4$, $p=0.00$		
(Range: −98.7 to 85.8)						AN twins > control twins, 11.37(−6.61 to 23.37)	$p=0.06$	($d=0.5$)
						BD twins > control twins, 20.69 (2.00–39.38)	$p=0.03^*$	($d=0.7$)
						Non-AN co-twins < control twins, −20.87 (−40.81 to 0.93)	$p=0.04^*$	($d=-0.8$)
						Non-BD co-twins > control twins, 20.69 (3.33–36.98)	$p=0.02^*$	($d=1.0$)
Difficulties in Emotion Regulation†	86.27 (29.40)	86.83 (31.16)	86.60 (20.72)	84.26 (30.67)	76.25 (16.72)	Wald Chi Square: 7.61, $df=4$, $p=0.11$		
(Range: 39 to 153)						AN twins > control twins, 10.02 (0.43–19.61)	$p=0.04^*$	($d=0.5$)
						BD twins > control twins, 10.58 (−1.14 to 22.30)	$p=0.08$	($d=0.5$)
						Non-AN co-twins > control twins, 16.35 (−1.27 to 21.96)	$p=0.08$	($d=0.5$)
						Non-BD co-twins > control twins, 8.01 (−14.12 to 30.14)	$p=0.48$	($d=0.5$)

Note:

NB: monozygotic twin pair whose proband had a diagnosis of eating disorder not otherwise specified-inappropriate compensatory behaviours was excluded from this analysis. AN twins: anorexia nervosa (anorexia nervosa-restricting type, anorexia-binge/purge type and eating disorder not otherwise specified-anorexia nervosa) monozygotic and dizygotic twins. BD twins: bulimic disorders (bulimia nervosa, eating disorder not otherwise specified-bulimia nervosa and binge eating disorder) monozygotic and dizygotic twins. Non-AN co-twins: monozygotic and dizygotic non-anorexia nervosa co-twins. Non-BD co-twins: monozygotic and dizygotic non-bulimic disorder co-twins. Controls twins: monozygotic and dizygotic twins.

Descriptive statistics presented are raw means and standard deviation (two decimal places).

†Data were analysed with the Depression Anxiety and Stress Scale (Lovibond & Lovibond, 1995) included as a covariate, Reading the Mind in the Eyes Test (Baron-Cohen et al., 2001), Emotion stroop task (Ashwin et al., 2006), and Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004).

*$p < 0.05$.

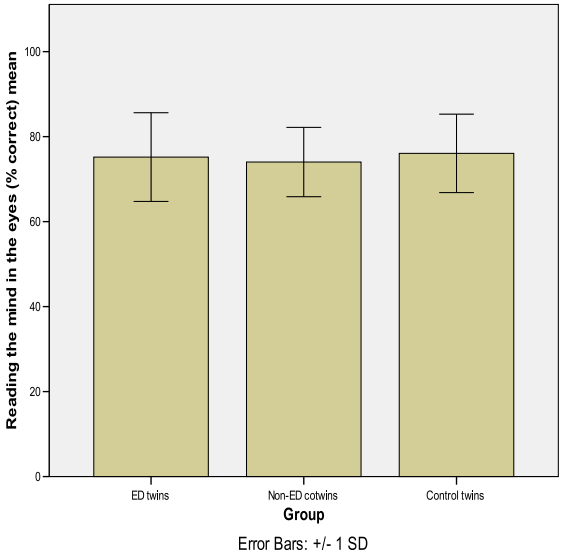

Figure 1. Emotion recognition in eating disorders and as a familial trait. Reading the Mind in the Eyes mean (% correct) (Baron-Cohen et al., 2001): Raw means and standard deviation presented

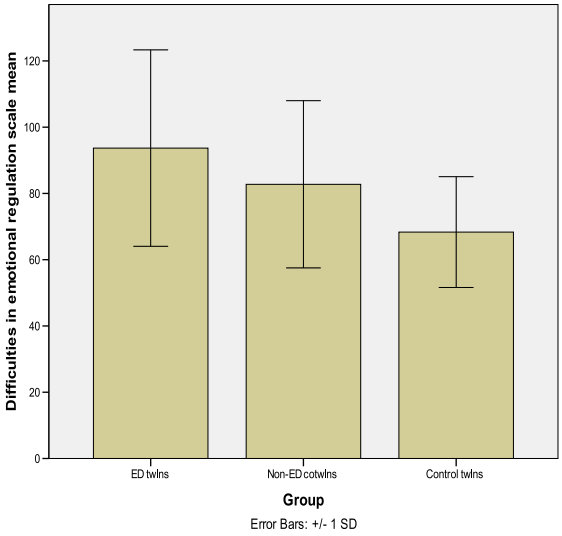

Figure 3. Difficulties in emotion regulation in eating disorders and as a familial trait. Difficulties in Emotion Regulation Scale mean (Gratz & Roemer, 2004): Raw means and standard deviation presented

Reading the Mind in the Eyes test (Baron-Cohen et al., 2001): Twins with eating disorders had less accuracy in emotion recognition in comparison with controls with a small effect size ($p = 0.59$, $d = -0.1$) at trend level (Table II). The impairment was more pronounced in twins with anorexia nervosa at trend level (small sized effect; $p = 0.23$, $d = -0.3$) in comparison with twins with bulimic disorders where it was not evident ($p = 0.98$, $d = 0$) (Table III). *Emotional Stroop task attentional bias* (Ashwin et al., 2006): Twins with eating disorders had greater attentional bias to social stimuli ($p = 0.40$ $d = 0.3$) at trend level (Table II). This effect was larger for twins with bulimic disorders ($p = 0.35$, $d = 0.4$) in comparison with twins with anorexia nervosa ($p = 0.69$, $d = 0.1$) (Table III).

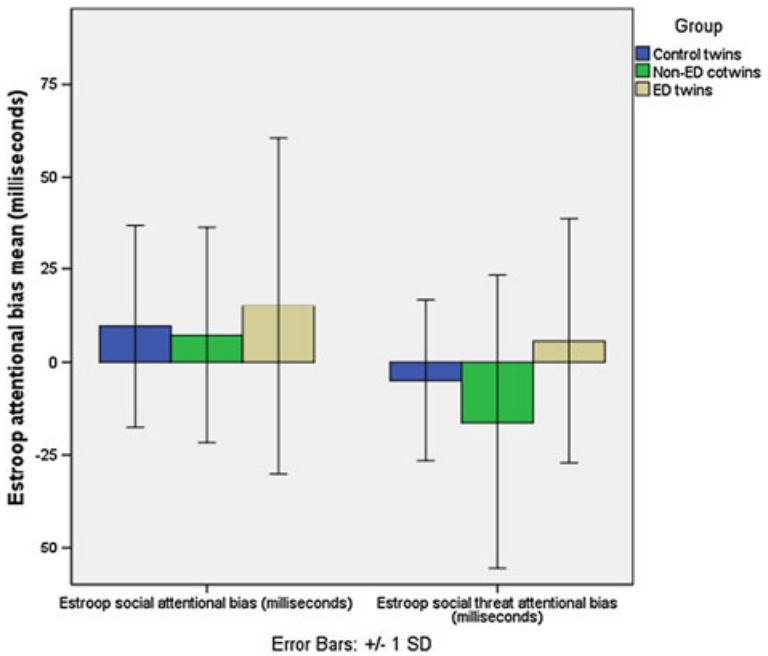

Figure 2. Social and social threat attentional bias in eating disorders and as a familial trait. Emotional Stroop task mean (milliseconds) (Ashwin et al., 2006): Raw means and standard deviation presented

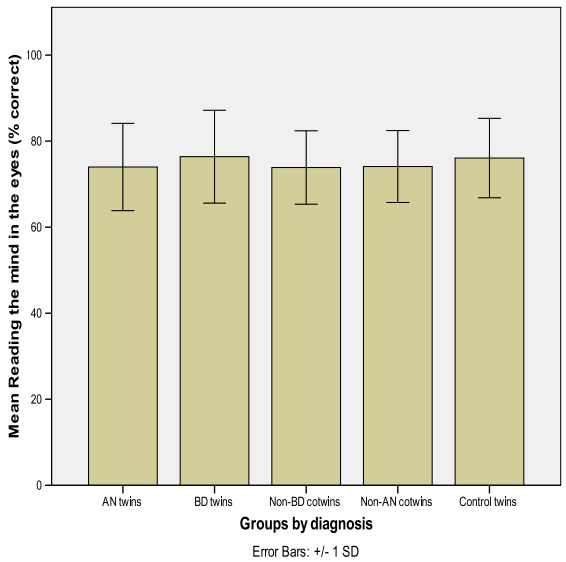

Figure 4. Emotion recognition for 'overall groups' sub-divided by eating disorder diagnosis and as a familial trait. Reading the Mind in the Eyes mean (% correct) (Baron-Cohen et al., 2001): Raw means and standard deviation presented

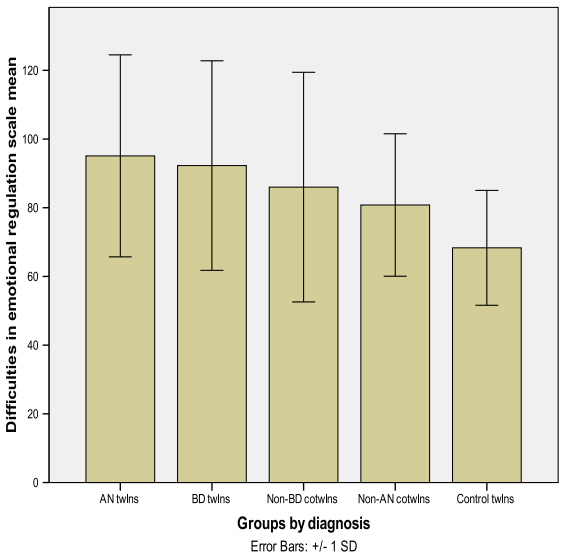

Figure 6. Difficulties in emotion regulation for 'overall groups' sub-divided by eating disorder diagnosis and as a familial trait. Difficulties in Emotion Regulation Scale mean (Gratz & Roemer, 2004): Raw means and standard deviation presented

In addition, twins with eating disorders had a significantly greater attentional bias to social threat (angry faces) ($p = 0.02$*, $d = 0.6$) in comparison with control twins (Table II). This was more pronounced in twins with bulimic disorders ($p = 0.03$*, $d = 0.7$) in comparison with twins with anorexia nervosa ($p = 0.06$, $d = 0.5$) (Table III).

Difficulties in Emotion Regulation (Gratz & Roemer, 2004): Twins with eating disorders had a significantly higher score in comparison with control twins ($p = 0.02$*, $d = 0.4$ (Table II), and there appeared to be no differences between twins with bulimic disorders ($p = 0.08$, $d = 0.5$) and twins with anorexia nervosa ($p = 0.04$*, $d = 0.5$) (Table III).

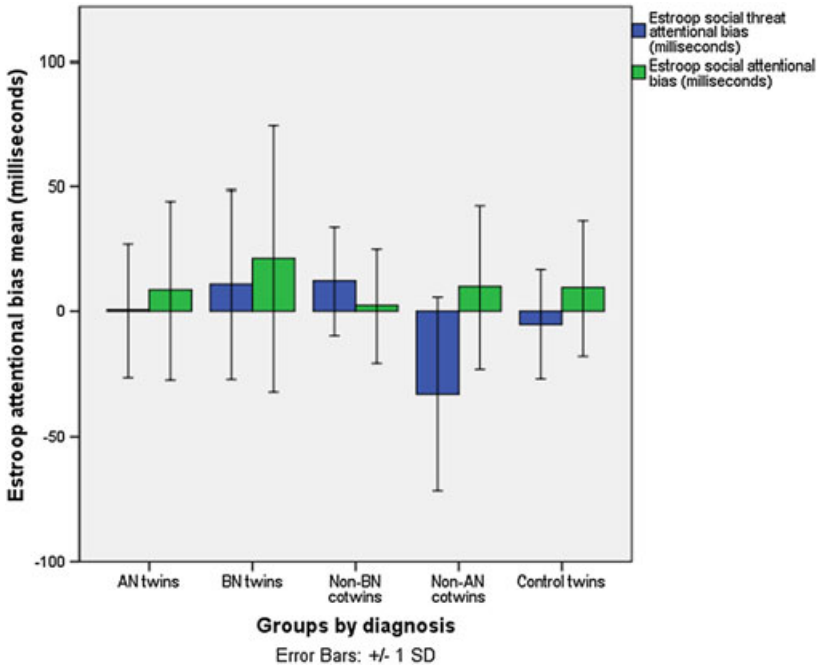

Figure 5. Social and social threat attentional bias for 'overall groups' sub-divided by eating disorder diagnosis and as a familial trait. Emotional Stroop task mean (milliseconds) (Ashwin et al., 2006): Raw means and standard deviation presented

(ii) Non-eating disorder co-twins *versus* control twins

Reading the Mind in the Eyes test (Baron-Cohen et al., 2001): Non-eating disorder co-twins had less accurate emotion recognition in comparison with control twins with a small effect size ($p = 0.69$, $d = -0.1$) at trend level (Table II). The difficulties were greater for non-bulimic disorder co-twins ($p = 0.36$, $d = -0.2$) in comparison with non-anorexia nervosa co-twins ($p = 0.70$, $d = -0.1$) (Table III).

Emotional Stroop task attentional bias (Ashwin et al., 2006): Non-eating disorder co-twins had attentional bias to social stimuli ($p = 0.75$, $d = 0.1$) at trend level (Table II). In this condition, there appeared to be opposite effects between diagnoses because non-anorexia nervosa co-twins supported the hypothesis and had attentional bias to social stimuli ($p = 0.49$, $d = 0.2$), whereas non-bulimic disorder co-twins had attentional bias to non-social stimuli ($p = 0.63$, $d = -0.2$) (Table III).

In the condition assessing attentional bias to social threat stimuli in non-eating disorder co-twins, there was attentional bias in the opposite direction, towards social neutral stimuli at trend level (Table II) ($p = 0.56$, $d = -0.2$). This transdiagnostic result may have been powered by non-anorexia nervosa co-twins who had attentional bias to social neutral stimuli ($p = 0.04^{*}$, $d = -0.8$). In contrast, non-bulimic disorder co-twins supported the hypothesis and demonstrated attentional bias to social threat stimuli ($p = 0.02^{*}$, $d = 1.0$) (Table III).

Difficulties in Emotion Regulation (Gratz & Roemer, 2004): For the Difficulties in Emotion Regulation Scale, non-eating disorder co-twins had a higher score in comparison with controls with a medium effect size ($p = 0.11$, $d = 0.5$) (Table II). There appeared to be no differences between non-anorexia nervosa co-twins ($p = 0.08$, $d = 0.5$) and non-bulimic disorder co-twins ($p = 0.48$, $d = 0.5$) (Table III).

Relationship of emotional processing to clinical features

For twins with eating disorders, a greater social attentional bias (measured by the Emotional Stroop task; Ashwin et al., 2006) was positively associated with the duration of bingeing [in months ($r = 0.44$, $p = 0.00^{**}$)] and number of years having been overweight ($r = 0.28$, $p = 0.05^{*}$).

Greater social threat attentional bias (measured by the Emotional Stroop task; Ashwin et al., 2006) was associated with a longer duration of vomiting [in months ($r = 0.34$, $p = 0.02^{*}$)] and the duration of laxative/diuretic use [in months ($r = 0.30$, $p = 0.04^{*}$)]. Emotional processing features were not significantly associated with any features in non-eating disorder co-twins or control twins.

In twins with eating disorders, greater difficulties in emotion regulation (Gratz & Roemer, 2004) were positively associated with a longer duration of fasting [in months ($r = 0.36$, $p = 0.02^{*}$)] and a lower number of years having been recovered ($r = -0.52$, $p = 0.00^{**}$).

Analysis of behavioural traits as heritable features in twins with eating disorders

The following analysis explores the endophenotype criteria of 'heritability' (Gottesman & Gould, 2003) in twins with eating disorders and their unaffected co-twins.

(i) Summary of emotion recognition (Reading the Mind in the Eyes test; Baron-Cohen et al., 2001) as a heritable trait in twins with eating disorders

In support of the hypothesis, monozygotic twins had significant within-pair similarity [$r = 0.47$ (CI: 0.1–0.74), $p = 0.01^{**}$] for emotion recognition in comparison with dizygotic twins [$r = 0.24$ (CI: −0.43 to 0.73), $p = 0.24$]. This suggests that this trait might be influenced by genetic effects.

(ii) Summary of social and social threat attentional bias (Emotional Stroop task; Ashwin et al., 2006) as heritable traits in twins with eating disorders

For social attentional bias, monozygotic twins had significant within-pair similarity [$r = 0.47$ (CI: 0.09–0.73; $p = 0.01^{**}$)]. This was not the case for dizygotic twins [$r = 0.11$, (CI: −0.67 to 0.53), $p = 0.63$], therefore suggesting a genetic basis to this trait.

For social threat attentional bias, monozygotic twins [$r = 0.2$ (CI: −0.15 to 0.60), $p = 0.1$] appeared to have greater within-pair similarity than dizygotic twins [$r = 0.06$ (CI: −0.56 to 0.64), $p = 0.43$], although it is noted that neither of these within-pair correlations reached statistical significance.

(iii) Summary of difficulties in emotion regulation (Difficulties in Emotion Regulation Scale; Gratz & Roemer, 2004) as a heritable trait in twins with eating disorders

For the Difficulties in Emotion Regulation Scale, neither monozygotic twin pairs [$r = 0.30$ (CI: −0.11 to 0.62), $p = 0.08$] nor dizygotic twin pairs [$r = 0.67$ (CI: 0.01–0.93), $p = 0.02$] had significant within-pair similarity. This suggests a stronger influence of environmental factors.

Discussion

This study examined whether aspects of emotional processing—emotion recognition (measured by the Reading the Mind in the Eyes test, Baron-Cohen et al., 2001), attentional biases to social and social threat stimuli (measured by the Emotional Stroop task, Ashwin et al., 2006) and difficulties in emotion regulation (measured by the Difficulties in Emotion Regulation Scale, Gratz and Roemer, 2003)—could be endophenotypes of eating disorders by using a genetically sensitive twin design. To our knowledge, this is the first study to explore these features in a twin sample with eating disorders. The initial endophenotype criteria for the emotional trait to be associated with the illness were met for all measures at trend level. Three of these traits—difficulties in emotion recognition, attentional bias to social threat and difficulties in emotion regulation—were found in their non-eating disorder co-twins at trend level, suggesting that they co-segregate within families. Lastly, emotion recognition and attentional bias to social stimuli appeared to be heritable. The low statistical power, particularly for comparisons between sub-groups, means that these findings are tentative and require further replication.

Difficulties in complex emotion recognition

Overall, twins with anorexia nervosa demonstrated the greatest difficulties in emotion recognition measured by the Reading the Mind in the Eyes test (Baron-Cohen et al., 2001). The effect size

($d = -0.3$) lies within the range found in the meta-analysis conducted by Oldershaw et al. (2011); $d = -0.5$ (95% CI -0.73 to -0.28). This finding coincides with a previous study that found greater difficulties in women with anorexia nervosa in comparison with those with bulimia nervosa (Harrison, Sullivan, et al., 2010). The findings are also comparable with studies of unaffected relatives of probands with autistic spectrum disorder (Baron-Cohen & Hammer, 1997; Losh & Piven, 2007) and schizophrenia (de Achával et al., 2010; Ibanez et al., 2010), which found it be a familial trait. When assessing the genetic basis of emotion recognition, there was support for the hypothesis, because monozygotic twins had significant within-pair similarity, whereas this was not the case for dizygotic twins.

Social attentional biases

In eating disorder twins, there was attentional bias to social and social threat stimuli with small to medium effect sizes. Both of these were more pronounced in twins with bulimic disorders in comparison to twins with anorexia nervosa. This is similar to a study by Harrison, et al. (2010), which found greater attentional biases to social stimuli in women with bulimia nervosa ($d = 0.8$) in comparison to those with anorexia nervosa ($d = 0.6$). Attentional biases to social and social threat stimuli was positively associated with the duration of bingeing, vomiting and laxative use. This supports the hypothesis that difficulties in emotional processing and sensitivity to interpersonal threat are linked to externalising strategies, such as binge eating, to regulate emotion (Aldao et al., 2010; Hartmann, Zeeck, & Barrett, 2010).

There was evidence of attentional bias to social threat stimuli being a familial trait because unaffected twins of those with a bulimic disorder also demonstrated this feature with a large effect size ($d = 1.0^{*}$). There was the opposite effect with non-anorexia nervosa co-twins, who displayed greater attentional bias to social neutral stimuli. Attentional bias to social stimuli appeared to have a more pronounced genetic basis in comparison with attentional bias to social threat.

Difficulties in emotion regulation

Lastly, difficulties in emotion regulation (Gratz and Roemer, 2003) were associated with the illness and present in the unaffected twin siblings suggesting that this is a familial trait.

Implications for treatment

The findings that difficulties in emotion recognition and attentional bias to social stimuli may have a stronger genetic basis than attentional bias to social threat stimuli could assist clinicians in assigning tailored goals for improvement. Traits with a substantial genetic basis such as emotion recognition may have a slower response to treatment and may require a form of remediation therapy. This may include emotional skills training (Money, Davies, & Tchanturia, 2011) or attentional bias modification treatment (Bar-Haim, 2010; Hakamata et al., 2010). Additional pharmacological treatments such as oxytocin may also be effective (Bos, Panksepp, Bluthé, & Honk, 2012).

Strengths and limitations

This study adopted the strong methodological design of a twin study to parse out the genetic and environmental factors that contribute to emotional processing in people with eating disorders. The high within-pair similarity for monozygotic twins confirmed the external validity of these emotional processing tasks because identical twins are to a large extent naturally controlled for age, gender, pre-adolescent socio-economic background and environmental experiences.

Furthermore, this study's analysis demonstrated that anomalies in the emotional phenotype exist in women with eating disorders, even when the effects of depression are controlled for. This may give weight to the etiological models of eating disorders, which propose that these emotional features are specific to the eating disorder phenotype and not simply a consequence of comorbid features such as depression and anxiety (Kaye, 2008; Treasure et al., 2012).

It is acknowledged that this study has a number of limitations, notably that the conclusions are constrained by low statistical power. Due to this being an exploratory study, it was chosen to report correlations that had not been corrected for multiple testing and highlight group comparisons that demonstrated a predicted trend but had not attained statistical significance. There were results that confirmed previous research, which suggests that the findings of emotional endophenotypes in twins can be generalised to singletons with eating disorders. However, these finding have their limitations, because the likelihood of having falsely rejected the null hypothesis was increased.

Secondly, the use of a cross-sectional design is taken into account when interpreting the findings. Eating disorders are known to be unstable longitudinally, which inevitably creates diagnostic difficulties for genetic studies using a cross-sectional design (Helder and Collier, 2011). For the practical purposes of recruiting a rare sample of twins with eating disorders, this study chose to recruit those with eating disorders across the spectrum and at various stages of the illness and recovery. One of the strengths of this research is that diagnosis was based on an account of eating disorder symptoms that had occurred across the life course as opposed to simply classifying them on the basis of a current category (Anderluh et al., 2003). However, by choosing to assess group differences between broad groups of anorexia nervosa and bulimic disorders that encompassed binge eating disorder, the findings may well have missed important features that characterise specific conditions. Previous research has shown that difficulties in emotion regulation may be an antecedent factor to binge eating in binge eating disorder (Munsch, Meyer, Quartier, & Willhelm, 2012), although less is known about the role of emotion recognition difficulties or social attentional biases in the development of binge eating disorder.

Thirdly, the largely recovered sample may account for the attenuated difficulties in emotional functioning, as found in previous research (Harrison, Tchanturia and Treasure, 2010). In addition, it was not feasible to explore whether the emotional profile of the restricting anorexia nervosa group ($n = 12$, 10.7%) was distinct from those with anorexia nervosa-binge/purge type and eating disorder not otherwise specified-anorexia nervosa, because this group was too small to analyse on its own. It is noted that not all the twins in the anorexia nervosa group were underweight, because this group included those with eating disorder not otherwise specified-anorexia nervosa. More generally, the eating disorder twins were a mix of those currently underweight

(11.8%, $n = 6$) and normal weight (88.2%), which may have influenced the findings. It is not possible to control for BMI because it is a clinical feature that is closely entangled with the symptoms of anorexia nervosa (Abbate-Daga et al., 2011). Therefore, it is difficult to determine whether it is the illness or a low BMI that contributes to performance on behavioural tasks. Notably, studies have had conflicting findings over the influence of BMI on neuropsychological performance (Mathias & Kent, 1998; Tenconi et al., 2010; Tchanturia et al., 2011).

Fourthly, attention is drawn to the non-eating disorder co-twins who were substantially older than the group of eating disorder twins and controls. Although age was included as a covariate, this factor may have contributed to findings in this group, since emotional processing deficits are known to increase with age as a consequence of deficits in executive function (Garcia-Rodriquez et al., 2011).

Lastly, there appeared to be wide variability in emotional processing abilities within groups. It may be plasticity (Belsky et al., 2009; Homberg & Lesch, 2011) or variation in the s-allele of 5-HTTLPR that accounts for enhanced emotional vigilance in some people but not others (Kaye, 2008; Pergamin-Hight et al., 2012). Future research could examine larger samples and conduct genetic studies or adopt other behavioural measures to determine the factors that create variance in emotional processing. Another method could be principal components of heritability, which has been previously used in the field of schizophrenia (Wiener et al., 2012). It seeks to compare how traits cluster within clinical and control families, to determine the genetic basis of each cluster and its correlation with the psychiatric disorder. Such research would clarify variation but would require larger samples of families with eating disorder probands.

Conclusions

The findings from this study are tentative, given the aforementioned limitations. However, they suggest that each aspect of emotional processing varies across the diagnostic spectrum with more difficulties in emotion recognition in anorexia nervosa and greater attentional bias towards social threat in bulimic disorder. There was also some evidence to support a familial or genetic basis to some elements of emotional processing. With this in mind, future studies with larger samples and those adopting longitudinal designs should be conducted to explore whether emotional processing difficulties are truly endophenotypes that lie between the clinical symptoms and the genes that confer risk.

Acknowledgements

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