RESEARCH ARTICLE

Altered Reward Reactivity as a Behavioural Endophenotype in Eating Disorders: A Pilot Investigation in Twins

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Abstract

Altered reward reactivity is a potential risk endophenotype for eating disorders (EDs). The aim of this study was to examine reward reactivity in female twins with EDs and compare it with a twin control group. A sample of 112 twins [$n = 51$ met lifetime DSM-IV ED criteria (anorexia nervosa $n = 26$; bulimic disorders $n = 24$), $n = 19$ unaffected cotwins and $n = 42$ control twins] was administered measures assessing reward reactivity, including the Game of Dice Task, the Behavioural Inhibition/Activation (BIS/BAS) Scales and the Appetitive Motivation Scale (AMS). Within pair, correlations for monozygotic and dizygotic twins were calculated and generalised estimating equations compared probands with non-ED cotwins and controls. The BAS and the AMS were reduced in EDs and negatively associated with restrictive symptoms. In addition, monozygotic twins pairs demonstrated significant within pair similarity for the BAS and AMS. Conversely, there was less evidence to support the BIS or risky decision-making as measured by the Game of Dice Task as an endophenotype in EDs. Copyright © 2017 John Wiley & Sons, Ltd and Eating Disorders Association.

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Keywords
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Introduction

Across the eating disorder (ED) spectrum, there is an altered balance between reward and inhibition (Wierenga et al., 2014). Altered reward sensitivity occurs in patients with opiate dependence (Brand, Roth-Bauer, Driessen, & Markowitsch, 2008), pathological gambling (Brand et al., 2005) and those with attention deficit hyperactivity disorder (Drechsler, Rizzo, & Steinhausen, 2009), binge ED (BED) (Svaldi, Brand, & Tuschen-Caffier, 2010) and bulimia nervosa (BN) (Brand, Frankie-Sievert, Jacoby, Markowitsch, & Tuschen-Caffier, 2007). However, in patients with anorexia nervosa (AN), altered reward sensitivity presents with symptoms of anhedonia, self-denial of food and other pleasures (Kaye et al., 2013), whereas those with BN display poor impulse control and engage in novelty seeking behaviours (Kaye et al.). Underlying these behaviours are alterations in the corticostriatal limbic and dorsal cognitive neural circuitry, which are systems involved in reward from food and self-control (Wierenga et al., 2014).

It has been difficult to determine whether alterations in reward reactivity are premorbid features, state-related or scars from the illness that persist after recovery (Frank, 2013). A further complication is that ED behaviours contribute to alterations in the brain's reward system, which may promote the illness and contribute to relapse (Frank). Genetically informative samples can help to inform whether altered reward reactivity is a premorbid feature by exploring whether the feature fulfils endophenotype criteria as defined by Gottesman and Gould (2003). Previous research using this paradigm of endophenotype criteria (Gottesman & Gould) has led to evidence that cognitive and emotional styles may be endophenotypes of EDs. For example, difficulties in set shifting appear to persist after recovery from AN indicating that it may have been premorbid to the illness (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005). Furthermore difficulties in set shifting and weak central coherence are familial traits that are present in unaffected sisters of those with EDs and research in twins indicates that these traits are heritable (Holliday et al., 2005; Kanakam, Raoult, Collier, & Treasure, 2012; Roberts, Tchanturia, & Treasure, 2010; Roberts, Tchanturia, & Treasure, 2013; Tenconi et al., 2010). Lastly, research in twins has shown that difficulties in emotion recognition and attentional biases to social stimuli are also present in unaffected twin siblings and heritable in people with EDs (Kanakam, Krug, Raoult, Collier, & Treasure, 2013). At this time, there have been limited studies examining whether reward reactivity is an endophenotype of EDs. As such, this study aims to investigate the endophenotype status

of altered reward reactivity measured by self-report measures and a neuropsychological task. The following sections will outline the current evidence base.

Self-report measures of reward reactivity in eating disorders

Studies using the Behavioural Inhibition/Activation (BIS/BAS) scales (Carver & White, 1994) have shown that people with EDs have higher levels of behavioural inhibition and lower levels of behavioural activation in comparison with controls (Harrison, O'Brien, Lopez, & Treasure, 2010; Harrison, Treasure, & Smillie, 2011). Similarly, the scores on the Appetitive Motivation Scale (AMS) are reduced in people with EDs (Harrison et al., 2011; Jackson & Smillie, 2005). There are also differences in reward reactivity across the ED spectrum, with AN being the least reactive to reward and associated with higher levels of behavioural inhibition and bulimic types being the most reactive to reward and having higher levels of behavioural activation (Harrison et al., 2011). This pattern appears to remain after recovery (Harrison et al., 2011).

The genetic basis or familial risk of altered reward reactivity measured by the BIS/BAS Scales (Carver & White, 1994) or the AMS (Jackson & Smillie, 2005) has not been assessed in people with EDs. Nevertheless, there is evidence from clinical ED samples that reward reactivity is a shared familial risk factor, which is present in unaffected sisters of those with AN (Karwautz, Rabe-Hesketh, Collier, & Treasure, 2002; Wade et al., 2008). However, unlike twin studies, which compare monozygotic (MZ) twins with dizygotic twins to determine the effects of heritability alone, familial studies cannot determine whether the similarities are due to non-shared environment, shared environment or genes.

Neuropsychological measures of reward reactivity in people with eating disorders

Gambling tasks may also be of clinical significance, because better decision-making is associated with great improvements in nutritional status in patients with AN following a cognitive behavioural treatment programme (Cavedini et al., 2006). A meta-analysis of 23 studies using the Iowa gambling task (IGT) indicated that people with EDs make disadvantageous choices with moderate to large effect sizes (Hedges' *g*: −0.72 in AN, −0.62 in BN and −1.26 in BED) (Guillaume et al., 2015). The review showed that participants with anorexia-purging (AN-P) type had lower net scores on the IGT compared with AN (Guillaume et al.). Individuals with BN demonstrated more risky decision-making on the Game of Dice Task (GDT) (Brand et al., 2005) in comparison with people with AN, AN-BP and healthy controls (Brand et al., 2007). Other bulimic disorders (BDs), such as BED, have demonstrated similar patterns of more risky decision-making on the task (Svaldi et al., 2010). Overall, there appears to be evidence that altered decision-making is associated with EDs.

There is limited research with regard to the endophenotype status of decision-making deficits measure by simulated gambling tasks. The previously mentioned meta-analysis of the IGT indicates that patients recovered from AN have similar scores to healthy controls, suggesting it may not be a premorbid feature (Guillaume et al., 2015). Genetically informative samples can also be useful in determining whether altered reward reactivity is a premorbid feature in the absence of longitudinal studies. One study that used genetically informative samples has shown that poor performance on the IGT is present in unaffected relatives of those with AN and influenced by genetic effects (heritability indices: 0.40), indicating that it is in part a premorbid feature (Galimberti et al., 2012).

The current study

The aim of the current study was to examine whether altered reward reactivity measured by the self-report measures: BIS/BAS (Carver & White, 1994), the AMS (Jackson & Smillie, 2005) and the neuropsychological task; GDT (Brand et al., 2005) fulfils the criteria for being an endophenotype. A twin sample provided a natural experiment to parse out the effects of genetic and environmental influences on the behaviour (Plomin, De Fries, McClearn, & McGuffin, 2001).

Three criteria used to define endophenotypes as outlined by Gottesman and Gould (2003, p.639) were investigated for reward sensitivity—(1) its 'heritability', by comparing MZ and dizygotic twins with the expectation that performance within MZ twin pairs will be more similar (i.e. significantly correlated) because they share 100% of genes, in comparison with dizygotic twin pairs who share only 50% of genes, on average (Plomin et al., 2001); (2) the 'co-segregation with the illness in families' by comparing their unaffected cotwins with controls twins; and (3) the 'association with the illness in the population': (i) by comparing the whole group of twins with EDs with control twins and (ii) by comparing probands with AN and BD with control twins.

Method

Ascertainment and recruitment

A total of 82 (73.2%) female twins with and without EDs from the St Thomas UK twin registry (www.twinsuk.ac.uk) (comprised of 12 000 twins representative of the general population) responded to a newsletter, advertising the study. Additional twins were recruited from a previous study conducted by Holland, Sicotte, and Treasure (1998) ($n = 14$, 12.5%). The remainder ($n = 16$, 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 16–60 years. Self-defined ethnicity indicated that the majority (91%) were White British. 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). The National Adult Reading Test (Table 1) indicated that no patient or control participant had clinical evidence of minor intellectual disability (Nelson & Wilson, 1991).

The ED sample included 16 twin pairs where both twins had a lifetime history of an ED (14, MZ and 2 dizygotic pairs) and 19 twin pairs where only one twin had a lifetime history of an ED (11 MZ and 8 dizygotic pairs). Therefore, in total, there were 51

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

	MZ-ED ($n = 39$)	MZ-non-ED ($n = 11$)	DZ-ED ($n = 12$)	DZ-non-ED ($n = 8$)	Control twins ($n = 42$)	Test statistic
Age	38.3 (14.5)	46.6 (16.8)	39.2 (14.6)	42.9 (16.9)	42.6 (12.8)	Wald χ^2: 7.3, *df*: 4, $p = 0.12$
Current BMI	21.6 (5.5)	22.3 (3.9)	21.2 (1.2)	22.7 (2.6)	22.5 (2.6)	Wald χ^2: 11.2, *df*: 4, $p = 0.02$
Lowest BMI attained throughout lifetime	16.9 (4.9)	19.5 (2.0)	16.9 (1.9)	18.8 (3.0)	—	Wald χ^2: 15.8, *df*: 3, $p = 0.00$
Highest BMI attained throughout lifetime	23.8 (4.6)	23.2 (6.1)	23.9 (3.7)	24.2 (6.3)	—	Wald χ^2: 0.3, *df*: 3, $p = 0.97$
Age of onset	17.5 (4.2)	—	19.9 (6.5)	—	—	—
Duration of illness (in years)	11.6 (11.4)	—	8.2 (10.5)	—	—	—
IQ estimated by the National Adult Reading Test	108.1 (8.9)	110.8 (8.7)	106.3 (10.4)	110.9 (7.7)	110.2 (7.2)	Wald χ^2: 3.8, *df*: 4, $p = 0.43$
Lifetime eating disorder type	Anorexia nervosa = 46.2%	—	Anorexia nervosa = 50%	—	—	—
	Bulimic disorder =56.4% Eating disorder not otherwise specified- inappropriate compensatory behaviours = 2.6%		Bulimic disorder =50%			
Recovered	56.4%	—	83.3%	—	—	—
BMI <18.5 (underweight)	15.4% ($n = 6$)		0% ($n = 0$)			
Years of recovery	10.03 (13.45) (range: 0–41)	—	11.08 (12.34) (range: 0–41)	—	—	—

Twins are separated on the basis of zygosity and clinical status.
Means and standard deviation in brackets (1.d.p.).
MZ-ED, monozygotic eating disorder twins; MZ-non-ED, monozygotic non-eating disorder cotwin; DZ-ED, dizygotic eating disorder twins; DZ-non-ED, dizygotic non-eating disorder cotwin.

twins who had a diagnosis of an ED and 19 unaffected cotwins. The probandwise concordance rate for a lifetime ED diagnosis was 72% in MZ twins and 33% in dizygotic twins.

From the group of twins who reported having an ED in their lifetime ($n = 51$), 62.8% ($n = 32$) reported that they were now recovered from their ED. Recovery was defined as having no behavioural or psychological symptoms associated with EDs for two or more years (Uher et al., 2003). In total, six twins were currently underweight, defined as having a body mass index (BMI) below 18.5.

Twins with EDs were separated by diagnosis into two broad groups (1) 'BD' ($n = 26$) [comprised of BN, ED not otherwise specified-BN (EDNOS-BN) and BED as proposed by Van den Eynde et al. (2011)] and (2) AN ($n = 24$) [including AN-restrictive (AN-R), AN-BP and EDNOS-AN] (American Psychiatric Association, 2000). One MZ twin with EDNOS-inappropriate compensatory behaviours was excluded from this grouping. In total, only 39.2% ($n = 20$) had received treatment.

Twenty-two patients in total experienced diagnostic crossover: 12 had a diagnosis of BN preceded by AN, 10 patients had a diagnosis of AN-BP or AN-P preceded by AN-R and 1 patient had a diagnosis of BN preceded by inappropriate compensatory behaviours. In total, 27 patients did not experience diagnostic crossover and had a stable diagnosis across the life course; 10 patients had a diagnosis of BN, 14 patients had a diagnosis of AN-R, 2 patients had a diagnosis of BED and 1 patient had a diagnosis of inappropriate compensatory behaviours.

The healthy control group included 17 MZ and four dizygotic twin pairs.

Exclusion and inclusion criteria

Twins were excluded if they had a visual impairment without a corrective aid, a neurological condition, a head injury, current epilepsy or an intelligence quotient (IQ) below 70 (measured by the National Adult Reading Test (Nelson & Wilson, 1991).

Clinical twins were included if they had a primary lifetime ED diagnosis (DSM-IV-TR criteria, 2002) or a history of EDNOS-inappropriate compensatory behaviours and their cotwin (unaffected or also with an ED) was able to participate. Because of the difficulties in recruiting twins with EDs, the present study included twins with ED in many different phases of the illness, such as those who were currently recovered.

Control twin pairs were included if both had a healthy BMI between 19 and 25 kg/m^2 and had no personal or family history of an ED 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)] 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, 1998)].

Clinical assessment

All twins with EDs and non-ED cotwins were interviewed using the EATATE (Anderluh, Tchanturia, Rabe-Hesketh, & Treasure, 2003) to obtain a lifetime history of ED symptoms and childhood obsessive-compulsive personality traits. It was administered by a trained doctoral researcher, and diagnosis was confirmed by a clinician. The semi-structured interview is comprised of a European adaptation of the Longitudinal Interval Follow-up Evaluation (Keller et al., 1987) and the Eating Disorders Examination Questionnaire Version (Fairburn & Cooper, 1993). It has been used previously in research of AN (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).

Patients were diagnosed on the basis of symptoms displayed over the life course. Longitudinal changes in diagnosis often occur. For example, a substantial number of patients with AN later develop BN and therefore it may be questioned whether it is appropriate to diagnose the patient as AN for research purposes (Micali et al., 2007). Therefore a hierarchical model of diagnosis was adopted whereby patients with BN irrespective of whether they had a previous history of AN, were classified as having a lifetime diagnosis of BN. This method was adopted by the Price Foundation Collaborative Group's genetic studies and in other familial risk studies in EDs (Kaye et al., 2000; Micali et al.). This is based on the premise that patients with BN are phenotypically different to patients with a lifetime diagnosis of AN (Micali et al.).

Self-report measures assessment of reward reactivity

The Behavioural Inhibition and Activation Scales (Carver & White, 1994)

The BIS/BAS (Carver & White, 1994) is a 20-item questionnaire designed to assess two general motivation systems of behaviours and affect. The BIS assesses the inhibition of behaviour due to fear of anxiety or punishment. The BAS assesses the responsiveness to reward cues. Participants are required to respond to each statement using a 4-point Likert scale ranging from 1 ('very true for me') to 4 ('very false for me'). In our sample, Cronbach's alpha was 0.75 for the BIS, 0.79 for the Behavioural Activation Reward Responsiveness Scale, 0.82 for the Behavioural Activation Drive Scale and 0.81 for the Behavioural Activation Fun-Seeking Scale.

The Appetitive Motivation Scale (Jackson & Smillie, 2005)

The AMS (Jackson & Smillie, 2005) is an 11-item measure of core reward reactivity, which reflects features similar to those measured by the BAS. It assesses the value felt from obtaining a reward as well as the motivation to approach ideas and physical stimuli. Participants are required to indicate to what extent they agree with each statement using a 4-point Likert scale ranging from 1 (strongly disagree) to 4 (strongly agree). In Jackson and Smillie's (2005) sample, the Cronbach alpha was 0.83 for the full scale indicating adequate internal consistency. In this sample, the Cronbach alpha was 0.77.

Experimental measures assessment of reward reactivity

Game of Dice Task (Brand et al., 2005)

The GDT (Brand et al., 2005) is a computerised task that measures decision-making under conditions of reward and punishment. By rolling the dice, participants can gamble virtual money. The outcome variable is the number of risky choices with a higher score indicating a more risky strategy. The task is described as having good convergent validity in that it has previously shown risky decision-making in patients with opiate dependence (Brand et al., 2008), pathological gambling (Brand et al.), attention deficit hyperactivity disorder (Drechsler et al., 2009), BED (Svaldi et al., 2010) and BN (Brand et al., 2007).

General assessment

The National Adult Reading Test (Nelson & Wilson, 1991) provides an indication of premorbid IQ. A greater number of incorrect pronunciations indicate a lower premorbid IQ. The outcome score correlates positively with overall performance on the British version of the Wechsler Adult Intelligence Scale (Crawford & Parker, 1998).

Procedure

Information and consent forms were sent prior to the appointment. Self-report questionnaires and diagnostic interviews were completed on the day of testing. This study was approved by the South London and Maudsley NHS Trust Research Ethics Committee.

Statistical methods

Intraclass correlation coefficients were calculated for MZ and dizygotic twins with EDs. These correlations analyse how strongly twin 1 resembles twin 2. Intraclass correlation coefficients could not be conducted for the control twin sample because the dizygotic control twin sample size was too small ($n = 8$).

For the familial analysis, differences between 'ED twins' (MZ and dizygotic probands), 'non-ED cotwins' (MZ and dizygotic non-ED cotwins) and control twins (MZ and dizygotic control twins) were analysed using the generalised estimating equation model for non-independent data (Liang & Zeger, 1986) (Table 2). This accounts for the correlative nature of twin pairs (i.e. controls for zygosity). A logarithm transformation was used for the GDT risky choices outcome variable because of this not being normally distributed. Age was included as a covariate throughout because age differed between groups although not at statistical significance. Depression and anxiety are highly comorbid with EDs; therefore, it can be difficult to tease these symptoms apart. For these reasons, similar research that has investigated reward sensitivity in EDs has chosen not to control for depression and anxiety (Svaldi et al., 2010; Brand et al., 2007). Therefore, to ensure that the findings of the present study could be

Table 2 Analysis of the reward reactivity in eating disorders and as a familial trait

	ED twins ($n = 51$)	Non-ED cotwins ($n = 19$)		Control twins ($n = 42$)	Group comparisons, mean difference (95% CI) p-value[†]	Cohens d	
Behavioural Inhibition Scale[†]	22.7 (3.5)	22.2 (3.7)	21.0 (2.7)	Wald $\chi^2 = 6.09$, $df = 2$, $p = 0.05$*			
				ED twins > control twins, 1.66 (0.34–2.97)	$p = 0.01$**	$d = 0.5$	Moderate
				Non-ED cotwins > control twins, 1.14 (−0.67 to 2.94)	$p = 0.51$	$d = 0.4$	Moderate
Behavioural Activation Scale[†]	12.2 (2.6)	12.2 (2.6)	13.3 (1.8)	Wald $\chi^2 = 6.7$, $df = 2$, $p = 0.04$*			
				ED twins < control twins, −1.12 (−2.14 to −0.28)	$p = 0.01$**	$d = -0.5$	Moderate
				Non-ED cotwins < control twins, −0.87 (−2.18 to 0.43)	$p = 0.19$	$d = -0.4$	Moderate
Appetitive Motivation Scale[‡]	30.1 (6.7)	30.4 (8.1)	31.8 (4.4)	Wald $\chi^2 = 3.78$, $df = 2$, $p = 0.15$			
				ED twins < control twins, −2.20 (−4.47 to 0.07)	$p = 0.06$	$d = -0.4$	Moderate
				Non-ED cotwins < control twins, −0.45 (−4.32 to 3.41)	$p = 0.82$	$d = -0.1$	Negligible
Game of Dice risky choices[§]	6.6 (4.9)	5.3 (4.5)	5.9 (4.9)	Wald $\chi^2 = 0.46$, $df = 2$, $p = 0.79$			
				ED twins = control twins, 0.05 (−0.11 to 0.21)	$p = 0.52$	$d = 0$	Negligible
				Non-ED cotwins = control twins, 0.02 (−0.16 to 0.21	$p = 0.81$	$d = 0$	Negligible

ED twins, monozygotic twins and dizygotic twins with eating disorders; non-ED cotwins, monozygotic and dizygotic non-eating disorder cotwins; controls twins, monozygotic and dizygotic twins.

Descriptive statistics presented are raw means and standard deviations (1 d.p).

[†]Data analysis about the Behavioural Inhibition Scale/Behavioural Activation Scale was analysed with age included as a covariate.

[‡]Data analysis about the Appetitive Motivation Scale was analysed with age included as a covariate.

[§]Data analysis about the Game of Dice Task (risky choices) was analysed after a logarithm transformation and age included as a covariate.

*$p < 0.05$.

**$p < 0.01$.

interpreted within a wider evidence base, it was also decided not to control for depression and anxiety. A second analysis was conducted using the generalised estimating equation model to compare diagnostic differences between AN and BD twins and their unaffected twin siblings with controls (Table 3).

To allow for accurate reporting of behaviour in this exploratory study of twins, outliers were not excluded from the analysis. This method for treating outliers replicates previous familial research into neuropsychological traits in people with EDs (Goddard & Treasure, 2013; Kanakam et al., 2013, 2012).

Performance was assessed separately for AN and BD groups (as defined in the participant section). Non-ED cotwins were separated on the basis of their probands diagnosis into the non-AN cotwins and non-BD cotwin groups. Because of the limited sample size for EDNOS-inappropriate compensatory behaviours ($n = 1$), this twin and her non-ED cotwin were excluded from the analysis (Table 3). Differences between the AN-R and AN-BP groups could not be explored statistically because these groups were too small.

Cohen's *d* effect sizes were calculated for each comparison with an effect size calculator, using descriptive statistics that were based on the age covariate. 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).

Spearman's Rho correlation coefficients assessed associations between the reward reactivity measures and the duration of clinical features in twins with EDs. In line with Rothman's (1990) argument, a correction for multiple testing was not required for group comparisons because the outcome variables were related. All analyses were carried out using PASW statistics version 22.0.

Sample size and power

The sample size in the present study was restricted by the number of twins with EDs it was possible to recruit. Because of the exploratory nature of this study, a *post hoc* power analysis was conducted using GPOWER software. This indicated that the present sample would have 47% and 14% power for detecting group differences between twins with BD or AN and controls at the 0.05 level for the GDT, respectively (Harrison, Macare, Cardi, Kanakam, & Treasure, 2012). In addition, the present sample would have 99% power for the BIS, 68% power for BAS (Harrison et al., 2011) and 94% power for the AMS (Jackson & Smillie, 2005) in detecting group differences between twins with EDs and controls at the 0.05 level.

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

Specific diagnosis (NB)	AN twins ($n = 24$)	BD twins ($n = 26$)	Non-AN cotwins ($n = 12$)	Non-BD cotwins ($n = 6$)	Control twins ($n = 42$)	Group comparisons, mean difference (95% CI) p-value[†]		Cohens d	
Behavioural Inhibition Scale[†]	23.2 (2.7)	22.2 (4.2)	21.3 (3.9)	24.32 (2.7)	21.0 (2.7)	Wald $\chi^2 = 14.33$, $df = 4$, $p = 0.01$**			
						AN twins > control twins, 1.63 (0.17–3.09)	$p = 0.03$*	$d = 0.5$	Moderate
						BD twins > control twins, 1.62 (−0.29 to 3.53)	$p = 0.10$	$d = 0.6$	Moderate
						Non-AN cotwins > control twins, 0.35 (−1.89 to 2.60)	$p = 0.76$	$d = 0.1$	Negligible
						Non-BD cotwins > control twins, 3.15 (1.27–5.03)	$p = 0.00$**	$d = 1.2$	Very large
Behavioural Activation Scale[†]	11.9 (2.8)	12.4 (2.5)	12.5 (3.1)	11.4 (1.3)	13.3 (1.8)	Wald $\chi^2 = 10.08$, $df = 4$, $p = 0.04$*			
						AN twins < control twins, −1.31 (−2.50 to −0.11)	$p = 0.03$*	$d = -0.6$	Moderate
						BD twins < control twins, −1.05 (−2.13 to 0.02)	$p = 0.05$*	$d = -0.6$	Moderate
						Non-AN cotwins < control twins, −0.64 (−2.50 to 1.20)	$p = 0.50$	$d = -0.2$	Small
						Non-BD cotwins < control twins, −1.50 (−2.13 to 0.02)	$p = 0.05$*	$d = -0.9$	Large
Appetitive Motivation Scale[‡]	29.5 (7.1)	29.6 (6.3)	31.2 (9.9)	29.3 (5.2)	31.8 (4.4)	Wald $\chi^2 = 4.94$, $df = 4$, $p = 0.29$			
						AN twins < control twins, −2.45 (−5.57 to 0.67)	$p = 0.12$	$d = -0.5$	Moderate
						BD twins < control twins, −1.97 (−4.69 to 0.75)	$p = 0.16$	$d = -0.4$	Moderate
						Non-AN cotwins = control twins, −0.01 (−5.42 to 5.40)	$p = 1.0$	$d = 0.0$	Negligible
						Non-BD cotwins < control twins, −1.06 (−6.89 to 4.78)	$p = 0.7$	$d = -0.2$	Small
Game of Dice risky choices[§]	6.2 (4.8)	6.7 (5.2)	6.1 (4.7)	2.7 (2.9)	5.9 (4.9)	Wald $\chi^2 = 7.33$, $df = 4$, $p = 0.13$			
						AN twins = control twins, −0.03 (−0.17 to 0.22)	$p = 0.79$	$d = 0$	Negligible
						BD twins > control twins, −0.05 (−0.12 to 0.23)	$p = 0.54$	$d = 0.3$	Small
						Non-AN cotwins > control twins, 0.13 (−0.06 to 0.32)	$p = 0.19$	$d = 0.3$	Small
						Non-BD cotwins < control twins, −0.22 (−0.49 to 0.04)	$p = 0.10$	$d = -0.5$	Moderate

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, monozygotic and dizygotic twins with anorexia nervosa (anorexia nervosa-restrictive, anorexia nervosa-binge purge and eating disorder not otherwise specified-anorexia nervosa); BD twins, monozygotic and dizygotic twins with bulimic disorders (bulimia nervosa, eating disorder not otherwise specified-bulimia nervosa and binge eating disorder); non-AN cotwins, monozygotic and dizygotic non-anorexia nervosa cotwins; non-BD cotwins, monozygotic and dizygotic non-bulimic disorder cotwins; controls twins, monozygotic and dizygotic control twins.

Descriptive statistics presented are raw means and standard deviation in brackets (1 d.p).

[†]Data analysis about the Behavioural Inhibition Scale/Behavioural Activation Scale was analysed with age included as a covariate.

[‡]Data analysis about the Appetitive Motivation Scale was analysed with age included as a covariate.

[§]Data analysis about the Game of Dice Task (risky choices) was analysed after a logarithm transformation and age included as a covariate.

*$p < 0.05$.

**$p < 0.01$.

Results

In Table 1, the ED twins, non-ED cotwins and controls were separated on the basis of zygosity and clinical status. There were no significant differences between the groups for age (Wald χ^2: 7.3, $df = 4$, $p = 0.12$) or IQ (Wald χ^2: 3.3, $df = 4$, $p = 0.51$). However, the groups were significantly different for BMI (Wald χ^2: 11.2, $df = 4$, $p = 0.02$), with unaffected twin sisters and control twins presenting with a higher BMI than twins diagnosed with a lifetime history of an ED.

The following analysis explores three endophenotype criteria as outlined by Gottesman and Gould (2003). The first is that the trait should be associated with the illness. Therefore, a correlational analysis was conducted to explore whether the behavioural

measures were predictive of clinical features. Furthermore, levels of reward reactivity were compared between ED twins and controls twins to explore whether the trait was associated with the illness. The second criteria was that the trait should co-segregate with the illness in families and therefore be present in the unaffected cotwins of those with EDs. Lastly, the third endophenotype criteria of 'heritability' (Gottesman & Gould, 2003) were explored in twins with EDs and their unaffected cotwins. It is expected that MZ twin pairs would have higher within pair similarity because they share 100% of genes, in comparison with dizygotic twin pairs who share only 50% of genes, on average (Plomin et al., 2001).

Tables 2 presents a comparison of measures assessing reward reactivity in ED twins, non-ED cotwins and controls, and Table 3 presents this comparison sub-divided by diagnosis.

Summary of the Behavioural Inhibition Scale (Carver & White, 1994) as associated with eating disorders, a familial and heritable trait

Higher scores on the BIS were associated with a lower 'current BMI' ($r = -0.30$, $p = 0.04$) and a lower 'lowest BMI' attained ($r = -0.30$, $p = 0.04$). The behavioural inhibition score was not significantly associated with any clinical features or age.

Overall twins with EDs had a significantly higher behavioural inhibition score in comparison with controls with a medium effect size ($d = 0.5$, $p = 0.01^{**}$) (Table 2). Non-BD cotwins had a significantly higher behavioural inhibition score in comparison with controls with a large effect size ($d = 1.2$, $p = 0.0$) (Table 3).

The MZ within-pair correlation [$r = 0.26$ (CI: −0.15 to 0.60) $p = 0.10$] for the BIS and the dizygotic within-pair correlation [$r = 0.52$ (CI: −0.16 to 0.85) $p = 0.06$] did not reach statistical significance, indicating limited genetic effects.

Summary of the Behavioural Activation Scale (Carver & White, 1994) as associated with eating disorders, a familial and heritable trait

A higher level of behavioural activation was associated with a lower duration of illness, [in years ($r = -0.42$, $p = 0.00$)], dieting [in months ($r = -0.35$, $p = 0.02$)], fasting [in months ($r = -0.44$, $p = 0.00$)] and laxative abuse [in months ($r = -0.29$, $p = 0.05$)] across the life course. In addition, higher levels of behavioural activation was associated with higher levels of appetitive motivation ($r = 0.75$, $p = 0.00$). Higher scores on the BAS were associated with a lower age ($r = -0.39$, $p = 0.01$).

Twins with EDs had a significantly lower behavioural activation score in comparison with controls with a medium effect size ($d = -0.5$, $p = 0.01^{**}$) (Table 2). Twins with AN ($d = -0.6$, $p = 0.03^{*}$) and BD ($d = -0.6$, $p = 0.05^{*}$) both had lower BAS scores in comparison with controls (Table 3). Non-BDs cotwins ($d = -0.9$, $p = 0.05^{*}$) had a significantly lower behavioural activation score in comparison with controls with a large effect size (Table 3).

Monozygotic twins had significant within-pair similarity [$r = 0.64$ (CI: 032–0.83) $p = 0.00^{**}$] for the BAS, suggesting that this trait might be influenced by genetic effects. However, this was not the case for dizygotic twins [$r = -0.39$ (CI: −0.82 to 0.33) $p = 0.86$].

Summary of the Appetitive Motivation Scale (Jackson & Smillie, 2005) as associated with eating disorders, a familial and heritable trait

Similar to reward reactivity measured by the BAS, higher scores on the AMS were associated with a lower duration of illness [in years ($r = -0.53$, $p = 0.00$)], dieting [in months ($r = -0.38$, $p = 0.01$)], fasting [in months ($r = -0.42$, $p = 0.00$)], laxative abuse [in months ($r = -0.39$, $p = 0.01$)] and number of years of having a BMI below 17.5. Higher scores on the AMS were also associated with a lower age ($r = -0.42$, $p = 0.00$).

There were no significant differences between groups indicating limited a familial contribution to this trait (Table 3).

For reward reactivity measured by the AMS, MZ twins had significant within-pair similarity, therefore suggesting a genetic basis to this trait [$r = 0.66$ (CI: 0.36–0.84) $p = 0.00^{**}$]. The dizygotic twin within-pair correlation did not demonstrate significant within pair similarity [$r = -0.74$ (CI: −0.93 to −0.20) $p = 0.99$].

Summary of the Game of Dice Task performance (Brand et al., 2005) as associated with eating disorders, a familial and heritable trait

Risky decision-making on the GDT was not significantly associated with any clinical features or age.

Overall, twins with EDs ($d = 0.0$, $p = 0.52$) and their non-ED cotwins ($d = 0.0$, $p = 0.81$) did not differ from controls for the number of risky choices made (Table 2).

For risky decision-making measured by the GDT, neither the MZ twin pairs [$r = 0.20$, (CI:−0.21 to 0.54), $p = 0.17$] nor the dizygotic twin pairs [$r = -0.07$ (CI: −0.65 to 0.56) $p = 0.58$] had significant within-pair similarity, indicating limited genetic effects.

Discussion

This study explored whether altered reward reactivity may be considered as an endophenotype of EDs by examining aspects of this trait in twins with EDs compared with control twins. Diagnostic differences were also explored between twins with BD that typically present with impulse control behaviours and twins with AN that are more likely to present with anhedonic symptoms (Kaye et al., 2013). Higher levels of behavioural inhibition and lower levels of reward reactivity (measured by the BAS) were found in twins with EDs (medium effect sizes). There was also evidence for a genetic basis to reward reactivity (measured by the BAS and AMS), but not for behavioural inhibition. There was little evidence to support GDT performance as a familial or genetic trait. Because of the low statistical power specifically for subgroup comparisons on the GDT, any conclusions for this measure should be regarded as tentative and further replication is needed.

Self-report measures of reward reactivity in eating disorders

Altered reward reactivity (measured by the BAS) fulfilled the endophenotype criteria, because it was elevated in twins with EDs and unaffected AN twins. The BAS also appeared to demonstrate within-pair similarity in MZ twins. However, behavioural inhibition was not found to be heritable, as there was no evidence for significant within pair similarity in MZ twins with EDs [$r = 0.26$ (CI: −0.15 to 0.60) $p = 0.10$]. Comparatively, in a study

of healthy controls, genetic factors accounted for approximately one-third of the variance in the behavioural inhibition (34%) and behavioural activation traits (35%) (Takahashi et al., 2007). It could be that the genetic/environmental causes of behavioural inhibition differ between people with EDs and controls. Furthermore, behavioural inhibition may be a more complex trait than reward reactivity, because it includes two features of inhibition: 'top down' behavioural inhibition due to cognitive control or 'bottom up' suppression of behaviour due to fear of punishment (Nigg, 2000).

Higher behavioural activation and appetitive motivation scores were predictive of a lower duration of restrictive ED behaviours (i.e. fasting and dieting). This suggests that people who are more responsive to reward cues are less likely to engage in anhedonic behaviours such as dieting and use of compensatory behaviours such as fasting for prolonged periods of time. This supports research, which indicates that individuals with restrictive EDs have a superior ability to delay reward and that this difference between bulimic and restrictive disorders may be rooted in abnormalities in the dopamine system (Bailer et al., 2013; Kaye et al., 2013).

Neuropsychological measurement of reward reactivity

Overall, this study found minimal effects on the GDT ($d = 0$ to $d = 0.3$) compared with previous research, which found much larger effect sizes ($d = -0.5$ to -0.9) for risky decision-making in people with BN and BED (Brand et al., 2007; Svaldi et al., 2010). This could be accounted for by the present sample, which was a heterogeneous diagnostic case mix of people at various stages of the illness and recovery.

The present study's findings may also reflect the GDT's reduced sensitivity to detect differences in smaller clinical samples compared with the BIS/BAS self-report measure (Brand et al., 2005; Carver & White, 1994). This was indicated by the relatively low levels of statistical power attained by the GDT (BN: 47% and AN: 14%) compared with the BIS/BAS measures (BIS: 94%, BAS: 68%) and AMS (94%) (Brand et al.; Carver & White, 1994; Jackson and Smillie, 2005).

This study found little evidence for familial or genetic effects on the GDT performance. This differs from a study of people with AN and their unaffected sisters, which found familial factors to account for variation in performance on the IGT (Galimberti et al., 2012). The IGT and the GDT may differ in some of the cognitive and emotional sub-functions required for executing the task. In the GDT, participants are given explicit instructions about the monetary gains or losses associated with each choice. However, in the IGT, this is implicit. Therefore, differences might be accounted for by the different cognitive processes involved. The aforementioned diagnostic mix of recovered and EDNOS participants in the ED group may also in part account for difficulties in determining genetic influences. In addition, there were more MZ twins (15.4%) currently underweight (BMI <18.5) in comparison with the dizygotic (0%) group. Given the influence of ED behaviours on the brain's neurochemistry and endocrinological effects that exacerbate symptoms, it is inevitable that the largely recovered state of the present sample influenced the findings (Frank, 2013; Herpetz-Dahlmann, Holtkamp, & Konrad, 2012).

Limitations

There are limitations associated with the sample that was used. The limited sample size means that this study was exploratory and any conclusions are drawn tentatively. It was difficult to recruit control twins and twins where at least one participant had a clinically significant ED. This meant there was insufficient statistical power most notably for the group comparisons using the GDT. However, it is noted that previous research, which investigated diagnostic differences between AN and BD types on the GDT, also had comparably small sample sizes. For example, Brand et al. (2007) had only 15 patients in their clinical group of BN and 15 in their control group.

Compared with previous research investigating the features of altered reward reactivity in EDs (Svaldi et al., 2010; Harrison et al., unpublished data; Brand et al., 2007), the present study's sample was largely recovered, which restricts our comparisons with previous research. In addition, more MZ twins were currently ill (56.1% recovered) compared with dizygotic twins (83.3% recovered), which may have affected group comparisons. Nevertheless, the number of probands that were currently underweight (BMI < 18.5) was only marginally greater in the MZ group (14.6%) in comparison with the dizygotic (0%) group. Furthermore, it was decided to combine patients with BN and BED (47.2%) into an overarching BD group because these patients share the same symptomatology and because of the limited sample size of patients with BED ($n = 2$).

Third, the clinical sample was older in age than samples used in previous research into reward reactivity. This may have affected the findings especially because reward reactivity as measured by the BAS ($r = -0.39$, $p = 0.01$) and AMS ($r = -0.42$, $p = 0.00$) was found to reduce as age increased in the present study.

Fourth, in this study, we chose not to exclude those with depression and/or anxiety in our clinical sample, because of this being a common comorbidity in EDs. However, it is well acknowledged that depression and anxiety can amplify deficits in neurocognitive function, and this may have influenced our findings (McClintock, Husain, Greer, & Cullum, 2010; Owens, Stevenson, Hadwin, & Norgate, 2014).

Implications

The present study indicates that reduced reward reactivity (measured by the BAS and AMS) is a prognostic indicator of restrictive behaviours and that this feature has aspects that have a familial and/or heritable basis. As such, it may be suggested that reward reactivity is an endophenotype that has specific significance for the risk and prognosis of EDs. Previous research has already shown the value of using other neuropsychological assessments in determining prognosis. For example, poor cognitive flexibility measured by the Brixton task and Wisconsin Card Sorting Test was found to be associated with a longer duration of illness and more severe ED rituals (Roberts et al., 2010).

Conclusions

The present study aimed to examine whether aspects of reward reactivity could be considered as an ED endophenotype. The findings suggest that higher reward sensitivity may protect against prolonged periods of restrictive ED behaviours. Furthermore, reward reactivity

measured by the BAS was reduced in ED twins and their unaffected twins. In addition, MZ twin pairs demonstrated significant within pair similarity. Conversely, there was less evidence to support a strong familial or genetic basis to measures, which require a balance between 'top down' control (cognitive inhibition) and 'bottom up' processes (impulses to emotion and reward), such as the BIS or the GDT. Because of the evolving nature of inhibitory processes and reward reactivity with time and as a consequence of disrupted eating patterns, future studies could adopt longitudinal designs as well as larger samples to explore and confirm the present study's findings.

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REFERENCES

Anderluh, M. B., Tchanturia, K., Rabe-Hesketh, S., & Treasure, J. (2003). Childhood obsessive-compulsive personality traits in adult women with eating disorders: Defining a broader eating disorder phenotype. *American Journal of Psychiatry*, *160*, 242–247.

Anderluh, M. B., Tchanturia, K., Rabe-Hesketh, S., Collier, D., & Treasure, J. (2009). Lifetime course of eating disorders: Design and validity testing of a new strategy to define the eating disorders phenotype. *Psychological Medicine*, *39*(1), 105–114.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders IV-revised (DSM) (Vol. IV--TR)*. Washington DC: American Psychiatric Press Inc.

Bailer, U., Frank, G., Price, J., Meltzer, C., Becker, C., & Mathis, C. (2013). Interaction between serotonin transporter and dopamine D2/D3 receptor radioligand measures is associated with harm avoidant symptoms in anorexia and bulimia nervosa. *Psychiatry Research*, *211*, 160–168. 10.1016/j.pscychresns.2012.06.010.

Brand, M., Frankie-Sievert, C., Jacoby, G. E., Markowitsch, H. J., & Tuschen-Caffier, B. (2007). Neuropsychological correlates of decision making in patients with bulimia nervosa. *Neuropsychology*, *21*, 74–750. 10.1037/0894-4105.21.6.742.

Brand, M., Fujiwara, E., Borsutzky, S., Kalbe, E., Kessler, J., & Markowitsch, H. J. (2005). Decision-making deficits of korsakoff patients in a new gambling task with explicit rules: Associations with executive functions. *Neuropsychology*, *19*, 267–277.

Brand, M., Roth-Bauer, M., Driessen, M., & Markowitsch, H. J. (2008). Executive functions and risky decision-making in patients with opiate dependence. *Drug and Alcohol Dependence.*, *97*, 64–72.

Carver, S. C., & White, L. T. (1994). Behavioural inhibition, behavioural activation, and affective responses to impending reward and punishment: The BIS/BAS scales. *Journal of Personality and Social Psychology*, *67*, 319–333.

Cavedini, P., Zorzi, C., Bassi, T., Gorini, A., Baraldi, C., & Ubbiali, A. (2006). Decision-making functioning as a predictor of treatment outcome in anorexia nervosa. *Psychiatry Research*, *145*, 179–187.

Crawford, J. R., & Parker, D. M. (1998). Prediction of WAIS IQ with the National Adult Reading Test: Cross-validation and extension. *The British Journal of Clinical Psychology*, *28*, 267–273.

Drechsler, R., Rizzo, P., & Steinhausen, H.-C. (2009). Decision making with uncertain reinforcement in children with attention deficit/hyperactivity disorder (ADHD). *Child Neuropsychology*, *16*, 145–161. 10.1080/09297040903190774.

Fairburn, C., & Cooper, Z. (1993). The eating disorder examination. In C. G. Fairburn, & C. G. Wilson (Eds.), *Binge eating: Nature, assessment and treatment* (, pp. 317–331). New York: Guilford Press.

Foa, E. B., Huppert, J. D., Susanne, L., Robert, L., Rafael, K., Greg, H., et al. (2002). The obsessive-compulsive inventory: Development and validation of a short version. *Psychological Assessment*, *14*, 485–496.

Frank, G. (2013). Altered brain reward circuits in eating disorders: Chicken or egg? *Current Psychiatry Reports*, *15*. 10.1007/s11920-013-0396-x.

Galimberti, E., Fadda, E., Cavallini, M. C., Martoni, R. M., Erzegovesi, S., & Bellodi, L. (2012). Executive functioning in anorexia nervosa patients and their unaffected relatives. Psychiatry research. Advance online publication. *Psychiatry Research*. 10.1016/j.psychres.2012.10.001.

Goddard, E., & Treasure, J. (2013). Anxiety and social-emotional processing in eating disorders: Examination of family trios. *Cognitive Therapy and Research*, *37*, 890–904.

Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. *The American Journal of Psychiatry*, *160*, 636–645.

Guillaume, S., Gorwood, P., Jollant, F., Van den Eynde, F., Courtet, P., & Richard-Devantoy, S. (2015). Impaired decision-making in symptomatic anorexia and bulimia nervosa patients: A meta-analysis. *Psychological Medicine*, *45*, 3377–3391.

Harrison, A., Macare, C., Cardi, V., Kanakam, N., & Treasure, J. (2012). Experimental measurement of reward sensitivity and impulsivity in eating disorders. (in preparation)

Harrison, A., O'Brien, N., Lopez, C., & Treasure, J. (2010). Sensitivity to reward and punishment in eating disorders. *Psychiatry Research*, *177*, 1–11. 10.1016/j.psychres.2009.06.010.

Harrison, A., Treasure, J., & Smillie, L. D. (2011). Approach and avoidance motivation in eating disorders. *Psychiatry Research*, *188*, 396–401. 10.1016/j.psychres.2011.04.022.

Herpetz-Dahlmann, B., Holtkamp, K., & Konrad, K. (2012). Eating disorders: Anorexia and bulimia nervosa, in. *Handbook of Clinical Neurology*, 447–459.

Holland, A. J., Sicotte, N., & Treasure, J. (1998). Anorexia nervosa: Evidence for a genetic basis. *Journal of Psychosomatic Research*, *32*, 561–571. 10.1016/0022-3999(88)90004-9.

Holliday, J., Tchanturia, K., Landau, S., Collier, D., & Treasure, J. (2005). Is impaired set-shifting an endophenotype of anorexia nervosa? *American Journal of Psychiatry*, *162*, 2269–2275. 10.1176/appi.ajp.162.12.2269.

Jackson, C. J., & Smillie, L. D. (2005). The appetitive motivation scale and other BAS measures in the prediction of approach and active avoidance. *Personality and Individual Differences*, *38*, 981–998. 10.1016/j.paid.2004.09.013.

Kanakam, N., Krug, I., Raoult, C., Collier, D., & Treasure, J. (2013). Social and emotional processing as a behavioural endophenotype in eating disorders: A pilot investigation in twins. *European Eating Disorders Review*, *21*, 294–307.

Kanakam, N., Raoult, C., Collier, D., & Treasure, J. (2012). Set shifting and central coherence as neurocognitive endophenotypes in eating disorders: A preliminary investigation in twins. *The World Journal of Biological Psychiatry*. 10.3109/15622975.2012.665478.

Karwautz, A., Rabe-Hesketh, S., Collier, D., & Treasure, J. (2002). Pre-morbid psychiatric morbidity, comorbidity and personality in patients with anorexia nervosa compared to their healthy sisters. *European Eating Disorders Review*, *104*, 255–270. 10.1002/erv.476.

Kaye, W. H., Lilenfeld, L. R., Berrettini, W. H., Strober, M., Devlin, B., Klump, K. L., et al. (2000). A search for susceptibility loci for anorexia nervosa: Methods and sample description. *Biological Psychiatry.*, *47*(9), 794–803. 10.1016/S0006-3223(99)00240-1.

Kaye, W., Wierenga, C., Bailer, U., Simmons, A., Wagner, A., & Bischoff-Grethe, A. (2013). Does a shared neurobiology for foods and drugs of abuse contribute to extremes of food ingestion in anorexia and bulimia nervosa? *Biol. Psychiatry*, *73*, 836–842. 10.1016/j.biopsych.2013.01.002.

Keller, M. B., Lavori, P. W., Friedman, B., Nielsen, E., Endicott, J., McDonald-Scott, P., et al. (1987). The longitudinal interval follow-up evaluation: A comprehensive method for assessing outcome in prospective longitudinal studies. *Archives of General Psychiatry.*, *44*, 540–548.

Liang, K.-Y., & Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika*, *73*, 13–22.

Lovibond, S. H., & Lovibond, P. F. (1998). Manual for the depression anxiety stress scales. *Psychology Foundation,* Syndey.

McClintock, S. M., Husain, M. M., Greer, T. L., & Cullum, C. M. (2010). Association between depression severity and neurocognitive function in major depression disorder: A review and synthesis. *Neuropsychology*, *24*(1), 9–34.

Micali, N., Holliday, J., Karwautz, A., Haidvogl, M., Wagner, G., Fernandez-Aranda, F., et al. (2007). Childhood eating and weight in eating disorder: A multi-centre European study of affected women and their unaffected sisters. *Psychotherapy and Psychosomatics.*, *76*, 234–241. 10.1159/000101502.

Nelson, H. E.,& Wilson, J. R. (1991). National Adult Reading Test (NART). *Test manual* (2nd ed.). Windsor, UK: NFER-Nelson.

Nigg, J. T. (2000). On inhibition/disinhibition in developmental psychopathology: Views from cognitive and personality psychology and a working inhibition taxonomy. *Psychological Bulletin*, *162*, 220–246.

Owens, M., Stevenson, J., Hadwin, J. A., & Norgate, R. (2014). When does anxiety help of hinder cognitive test performance? The role of working memory capacity. *British Journal of Psychology.*, *105*, 92–101. 10.1111/bjop.12009.

Peeters, H., Van Gestel, S., Vlietinck, R., Derom, C., & Derom, R. (1998). Validation of a telephone zygosity questionnaire in twins of known zygosity. *Behavior Genetics*, *28*, 159–163. 10.1023/a:1021416112215.

Plomin, R., De Fries, J. C., McClearn, G. E., & McGuffin, P. (2001). *Behavioral genetics* (4th ed.,). New York: Worth Publishers.

Roberts, M., Tchanturia, K., & Treasure, J. (2010). Exploring the neurocognitive signature of poor set-shifting in anorexia and bulimia nervosa. *J Psychiat Res*, *44*, 964–970.

Roberts, M., Tchanturia, K., & Treasure, J. (2013). Is attention to detail a similarly strong candidate endophenotype for anorexia nervosa and bulimia nervosa? *The World Journal of Biological Psychiatry*, *14*, 452–456.

Rothman, K. J. (1990). No adjustments are needed for multiple comparisons. *Epidemiology*, *1*, 43–46.

Stice, E., Telch, C., & Rizvi, S. (2000). Development and validation of the eating disorder diagnostic scale: A brief self-report measure of anorexia nervosa, bulimia, and binge eating disorder. *Psychological Assessment*, *12*, 123–131.

Svaldi, J., Brand, M., & Tuschen-Caffier, B. (2010). Decision-making impairments in women with binge eating disorder. *Appetite*, *54*, 84–92. 10.1016/j.appet.2009.09.010.

Takahashi, Y., Yamagata, S., Kijima, N., Shigemasu, K., Ono, Y., & Ando, J. (2007). Continuity and change in behavioral inhibition and activation systems: A longitudinal behavioral genetic study. *Personality and Individual Differences*, *43*, 1616–1625. 10.1016/j.paid.2007.04.030.

Tenconi, E., Santonastaso, P., Degortes, D., Bosello, R., Titton, F., Mapelli, D., et al. (2010). Set- Shifting abilities, central coherence, and handedness in anorexia nervosa patients, their unaffected siblings and healthy controls: Exploring putative endophenotypes. *World J Bio Psychia*, *11*, 813–823.

Uher, R., Brammer, M. J., Murphy, T., Campbell, I. C., Ng, V. W., Williams, S. C. R., et al. (2003). Recovery and chronicity in anorexia nervosa: Brain activity associated with differential outcomes. *Biological Psychiatry*, *54*, 934–942. 10.1016/s0006-3223(03)00172-0.

Van den Eynde, F., Guillaume, S., Broadbent, H., Stahl, D., Campbell, I. C., Schmidt, U., et al. (2011). Neurocognition in bulimic eating disorders: A systematic review. *Acta Psychiatrica Scandinavica*, *124*, 120–140. 10.1111/j.1600-0447.2011.01701.x.

Wade, T. D., Tiggeman, M., Bulik, C. M., Fairburn, C. G., Wray, N. R., & Martin, N. G. (2008). Shared temperament risk factors for anorexia nervosa: A twin study. *Psychosomatic Medicine*, *70*, 239–244. 10.1097/PSY.0b013e31815c40f1.

Wierenga, C. E., Ely, A., Bischoff-Grethe, A., Bailer, U. F., Simmons, A. N., & Kaye, W. H. (2014). Are extremes of consumption in eating disorders related to an altered balance between reward and inhibition? *Frontiers in Behavioral Neuroscience*, *8*, 410.