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## **An examination of central coherence in eating disorders and its clinical implications**

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**AN EXAMINATION OF CENTRAL COHERENCE IN EATING  
DISORDERS AND ITS CLINICAL IMPLICATIONS**

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**King's College London, University of London**

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## ABSTRACT

Eating disorders (ED) are complex psychiatric illnesses whose aetiology and maintenance involve the interaction of environmental, psychological and biological factors. A neurodevelopmental model for ED has been proposed in which anomalies in the neural template may manifest as disturbances in informational processing, such as rigidity and extreme attention to detail.

The purpose of this thesis was to advance the understanding of these cognitive anomalies that may be involved in the development and maintenance of ED.

A comprehensive examination of a neuropsychological trait called **weak central coherence**, a bias towards local over global processing, under the umbrella of an endophenotype approach and its clinical implications was proposed.

Two objectives were defined: to explore (1) whether weak central coherence fulfilled the first two criteria for an endophenotype i.e. to be present in people affected with the illness and after recovery, and (2) how findings from neuropsychological studies can be translated into clinical interventions.

To address the first objective, cognitive performance of women with current or past ED and healthy women was compared on a range of neuropsychological tests measuring either global or local processing abilities. To address the second objective, two pilot studies to measure the effectiveness and acceptability of novel modalities of treatment developed to address difficulties in global processing (cognitive remediation therapy and motivational enhancement feedback) based on neuropsychological assessment were carried out.

The results of this thesis provided evidence to suggest that weak central coherence might be an endophenotype for least a sub-group of the ED spectrum as it was present in women with current and past ED. Also, results showed that cognitive assessments and targeted interventions based on principles of cognitive remediation are highly valued and acceptable by patients and can be incorporated into standard care. Implications of these findings for future research and clinical practice are discussed.

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Carolina López

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## COMMON ABBREVIATIONS USED THROUGH THE THESIS

AN	Anorexia Nervosa
AQ	Autistic Spectrum Quotient
ASD	Autistic Spectrum Disorders
BMI	Body Mass Index
BN	Bulimia Nervosa
BPAN	Anorexia Nervosa Binge-Purge sub-type
CRT	Cognitive Remediation Therapy
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4 <sup>th</sup> Edition
ED	Eating Disorder or Eating Disorders
EDNOS	Eating Disorders Not Otherwise Specified
EDRec	Women recovered from an eating disorder
EDU	Eating Disorders Unit
EFT	Embedded Figures Test
GEFT	Group Embedded Figures Test
HADS	Hospital Anxiety and Depression Scale
HC	Healthy Control
HRT	Homograph Reading Task
IoP	Institute of Psychiatry
KCL	King's College London
MFFT	Matching Familiar Figures Test
NART	National Adult Reading Test
NPBN	Bulimia Nervosa Non-Purging sub-type
OA	Object Assembly
OCD	Obsessive Compulsive Disorders
OCI-R	Obsessive – Compulsive Inventory Revised Version
OCPD	Obsessive-Compulsive Personality Disorders
PBN	Bulimia Nervosa Purging sub-type
RAN	Anorexia Nervosa Restricting sub-type
RCFT	Rey-Osterrieth Complex Figure Test
SCT	Sentence Completion Task
Un/seg BD	Un/Segmented Block Design Test
WAIS	Wechsler Adult Intelligence Scale
WAIS-III	Wechsler Adult Intelligence Scale 3 <sup>rd</sup> edition
WISC	Wechsler Intelligence Scale for Children
WRAN	Weight-recovered women following a period of acute AN

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## THESIS OUTLINE

The purpose of the present thesis was to advance the understanding of the aetiological and maintaining factors of eating disorders in order to inform novel treatment interventions and also to give directions for future research. A comprehensive examination of a neuropsychological trait called **weak central coherence** within an endophenotype approach was proposed.

To address the overall objective, the work described in this thesis was comprised of 6 studies which (1) examined the theoretical and scientific evidence to postulate weak central coherence as a relevant cognitive trait in the study of eating disorders, particularly in anorexia nervosa, (2) explored whether people with current or past eating disorders present abnormalities in central coherence manifested in a bias towards detailed-focused processing, (3) investigated the relationship between weak central coherence and autistic-like personality traits, and (4) preliminarily explored how neuropsychological findings could be translated into clinical interventions.

A general outline of this thesis with a brief description of the contents by chapter is provided below.

Chapter 1: *Eating disorders and central coherence: defining concepts*. This chapter provides the conceptual and theoretical base for the development of the study proposed in this thesis. The definitions of the concepts in the way they were understood and used through this work are provided (e.g. weak central coherence, endophenotypes).

Chapter 2: *Central coherence in eating disorders: A systematic review*. This chapter provides a systematic review of the neuropsychological literature relevant to the study of weak central coherence in eating disorders. Specifically, this chapter summarises the evidence from controlled studies related to global and detail-focused cognitive styles in eating disorders. Also, this chapter highlights the gaps in the literature in the field of interest setting the scene for systematically addressing the hypothesis of weak central coherence as an endophenotype for eating disorders.

Chapter 3: *General methodology and materials*. This chapter addresses the rationale behind the selection of the methodology for the empirical work described in this thesis. This chapter outlines the research design, recruitment and data collection

procedures and general methods of analysis relevant for the work performed in this thesis.

Chapter 4: *An examination of central coherence in women with anorexia nervosa*. This chapter describes the first empirical study of this thesis, which explored the concept of central coherence in women with a current diagnosis of anorexia nervosa using a battery of five neuropsychological tasks measuring aspects of central coherence. This key study described how the hypothesis that women with current AN have weaker central coherence than healthy controls was addressed and the implications of these findings.

Chapter 3: *Weak central coherence across diagnosis: Is this cognitive style relevant for bulimia nervosa?* This chapter describes the second empirical study of this thesis that was aimed at examining the concept of central coherence in women with bulimia nervosa and addresses the similarities and differences with those with anorexia nervosa. Through the completion and results of this study, the first criterion required to define weak central coherence as an endophenotype was tackled.

Chapter 6: *Weak central coherence in women recovered from an eating disorder: state or trait effect?* The objective of this chapter was to investigate whether weak central coherence is a trait or state effect by examining this cognitive style in people recovered from an eating disorder. This chapter represents the final step in the preliminary exploration of weak central coherence as an endophenotype candidate for eating disorders (ED) according to the criteria stated by Gottesman and Gould's review for endophenotypes in psychiatry research (Gottesman and Gould, 2003).

Chapter 7: *From the details to the 'bigger picture'*. This chapter attempts to summarise the results from Chapters 4 to 6 with the overall objective of providing a 'bigger picture' of the weak central coherence in eating disorders. Some questions relevant to the understanding of the concept of central coherence in eating disorder are addressed such as whether central coherence is a unitary and universal concept and whether it relates to autistic-type traits in the eating disorder populations at all.

With Chapters 4 to 7 this thesis covered its first objective, which was to initiate the exploration of weak central coherence as an endophenotype for eating disorders, highlighting the importance of including this trait into the design of treatment interventions that target cognitive anomalies common in eating disorders.

Chapter 8 and 9 address the second main objective of this thesis: to examine how to translate the results from empirical studies on central coherence into clinical interventions. Specifically, this study explored the effectiveness of Cognitive Remediation Therapy (CRT) and a brief motivational feedback intervention on anomalies in central coherence in people with eating disorders.

Chapter 8: *The central coherence account translated into clinical practice: the development of a module of cognitive remediation therapy.* This chapter presents the preliminary development and implementation of a novel module of intervention specifically designed to target the concept of weak central coherence in the treatment of patients with severe anorexia nervosa. A description of principles underlying the development of CRT for anorexia nervosa is provided together with a general description of this module of intervention. Finally, the results of a pilot study that addressed the impact of CRT on the global processing difficulties of patients with severe anorexia nervosa is described. The study presented in this chapter forms part of a bigger project of CRT in anorexia nervosa led by Dr. Tchanturia.

Chapter 9: *The central coherence account translated into clinical practice: Part II. A brief motivational feedback intervention.* This chapter describes the aims, rationale, and procedures involved in the design of a novel intervention that translates the neuropsychological assessment of weak central coherence into a feedback module within the general new Maudsley model of treatment, specially designed for outpatient settings. Results of a pilot exploratory study that examined the viability and acceptance of such a module are presented. This work was jointly developed with Professor Treasure.

Chapter 10: *General conclusions: Achieving coherence.* This chapter endeavours to summarise the findings of this thesis and reviews the extent to which the research aims proposed for this thesis were met. Limitations are highlighted and guidelines for future research and clinical developments in central coherence in the eating disorders population derived from this work are discussed.

# 1 EATING DISORDERS AND CENTRAL COHERENCE: DEFINING CONCEPTS

## 1.1 Introduction to the chapter

The objective of this chapter is to describe the conceptual base of the present thesis. The chapter defines the main elements involved in the development of the hypothesis testing that will follow in the next chapters and the general model of understanding eating disorders (ED) that supports the development of the work presented in this thesis. Firstly, an overview of ED phenotypes (definition, classification and characteristics) is provided. This brief review is centred around the two main diagnostic categories of ED: Anorexia Nervosa (AN) and Bulimia Nervosa (BN). Secondly, a brief outline of the utility of the concept of endophenotypes in psychiatry in general and specifically in ED is described. Thirdly, the main concept under study in this thesis, the concept of **weak central coherence** is introduced. The origin of this concept in the field of autistic spectrum disorders (ASD) and its link with ED will be addressed, as well as the rationale and relevance to consider it as a candidate endophenotype of ED.

## 1.2 Eating Disorders Phenotypes

### 1.2.1 Introduction

Eating disorders (ED) are complex psychiatric disorders and can have severe consequences (Hudson *et al.*, 2007, van Hoeken *et al.*, 2003). The ED phenotype, i.e. the observable characteristics of the disorder that result from the combination between genetic and environmental factors involve a range of syndromes characterised by a primary and persistent disturbance of body image, associated with over or under control of eating and extreme behaviours related to weight control (e.g. food restriction) that results in a significant impairment of psychosocial and physical health (Fairburn and Harrison, 2003, Striegel-Moore and Bulik, 2007).

Eating disorders affect mainly, but not only, young females and have the highest rate of mortality linked to a psychiatric disorder in young age, due to medical

complications and suicide in chronic AN (Harris and Barraclough, 1998). Although more than half of diagnosed patients reach recovery (Lowe *et al.*, 2001) for those whose course is chronic, ED lead to devastating psychosocial and physical consequences for sufferers themselves (Steinhausen, 2002) and their families (Treasure *et al.*, 2005b). Also, the severe, recurrent course, and high level of physical complications associated with ED, involve a high economic cost for families and the public health care system (Office of Health Economics, 1994, Striegel-Moore *et al.*, 2007).

All these arguments highlight the importance to find appropriate and cost-effective treatments to alleviate sufferers of ED and their families. Unfortunately, the evidence with regards to treatment outcomes is so far unsatisfactory, especially for AN (NICE, 2004). It is hoped that developing evidence-based models of aetiology and maintenance factors can be translated into treatment for those suffering from an ED (Treasure, 2007, Treasure *et al.*, 2007a).

Eating disorders encompass psychological, physical, and environmental elements in their aetiology, development and maintenance (Collier and Treasure, 2004). However ED were conceptualised as being caused predominately by environmental and psychological factors during most of the second half of 20<sup>th</sup> century and the role of biology was then somewhat neglected. Towards the end of the 20<sup>th</sup> century, with the advance of new biotechnologies, the role of biology in the development of ED has been revisited. Indeed, the endophenotype concept has been incorporated into the discussion of ED aetiology in several ED reviews (Bulik *et al.*, 2007b, Steiger and Bruce, 2007, Treasure, 2007, Treasure *et al.*, 2007a). Currently there is an interest in looking at the neuro-psycho-biological basis of ED vulnerability.

### 1.2.2 Diagnostic Classification in Eating Disorders

There are two main international classifications relevant to EDs: the Diagnostic and Statistical Manual of the American Psychiatric Association currently in its fourth edition (DSM-IV: APA, 1994) and the International Classification of Disease of the World Health Organization (WHO, 1992) in its tenth edition (ICD-10). Broadly speaking, these classifications recognise three categories of ED, namely Anorexia Nervosa (AN), Bulimia Nervosa (BN), and Eating Disorders Not

Otherwise Specified (EDNOS). The latter includes sub-clinical AN and BN but also syndromes that are becoming more important in recent discussions about the taxonomy of ED, such as purging eating disorder (Keel, 2007) and binge eating disorder (BED) (Norrington and Palmer, 2005).

All ED disorders have in common core symptoms such as body dissatisfaction, preoccupation with food, weight and/or shape, and the use of unhealthy or extreme methods to control or reduce weight. Despite the aforesaid similarities, the disorders corresponding to the ED spectrum also have some particular clinical features to distinguish between each other. Whereas AN and BN are the main diagnostic categories with clear inclusion criteria and a detailed description of course and prognosis, EDNOS is a residual but no less important category which includes the vast majority of ED that do not fulfil the full criteria for AN or BN but will result in subtle functional impairment (Norrington and Palmer, 2005).

The conventional classification systems previously mentioned for EDs are today under an ongoing debate (Striegel-Moore and Wonderlich, 2007) which encompasses the growing knowledge of epidemiologic, genetic and psychobiological factors involved in the development and presentation of the disorders (Bulik *et al.*, 2007b).

For this thesis, the work will be centred in the traditionally defined main diagnostic categories of ED (AN and BN), as specified by the DSM-IV criteria, the most widely used classification for research purposes (Mezzich, 2002).

### ***1.2.2.1 Anorexia Nervosa***

Anorexia Nervosa is a complex and severe ED characterised by voluntary maintenance of weight under a healthy range through extreme means of controlling weight, such as over-exercise, restriction of food intake and purging behaviours, accompanied with an extreme fear of gaining weight or a denial of being low weight. It was described for the first time as a medical problem towards the end of the 17<sup>th</sup> century by Richard Morton (1694) who describe cases suffering from weight loss not associated to physical causes. Two centuries later, Lasegue (1873) and Gull (1874) illustrated two detailed cases that involved similar clinical characteristics to what is currently understood to be AN.

The current DSM-IV diagnostic criteria are displayed in Table 1.1. This classification includes two subtypes in response to the dichotomic clinical presentation, prognosis and responses to treatment of the AN cases: a *restricting subtype* (RAN) in which the sufferer does not engage in binge-eating or purging methods (e.g. vomiting, misusing laxatives or diuretics or enemas) as regular means of controlling or reducing weight; and a *binge eating/purging type* (BPAN) in which the sufferer regularly engages in binge-eating and purging behaviours.

The requirement of amenorrhoea (Criterion D) has been widely discussed due to both the evidence of patient who fulfil all the other criteria for AN but maintain regular menses (Garfinkel *et al.*, 1996) and the unstable relationship between weight loss and secondary amenorrhoea (Devlin *et al.*, 1989).

**Table 1.1 Current diagnostic criteria for AN according DSM-IV (1994)**

<b>Anorexia Nervosa</b>
A. Refusal to maintain body weight at or above a minimally normal weight for age and height (e.g. weight loss leading to maintenance of body weight less than 85 per cent of that expected; or failure to make expected weight gain during period of growing, leading to body weight less than 85 per cent of that expected)
B. Intense fear of gaining weight or becoming fat, event though underweight
C. Disturbance in the way in which the body weight or shape is experimented, undue influence of body weight or shape on self-evaluation, denial of the seriousness of the current low body weight
D. In postmenarcheal females, amenorrhoea, i.e. the absence of at least three consecutive menstrual cycles

Another common aspect of the phenotype of AN refers to the co-morbid conditions that are frequently associated with the illness. Psychiatric disorders, especially depression, anxiety and obsessive compulsive disorders (OCD) are often present in people with AN (Herzog *et al.*, 1992, Råstam, 1992, Råstam *et al.*, 2003, Speranza *et al.*, 2001). It has been argued that depression may be a consequence of starvation rather than a precedent or independent illness, whereas OCD seems to be more independent and many times precedes the onset of ED (Anderluh *et al.*, 2003, Collier and Treasure, 2004). Impulsive behaviours such as self-harm and substance abuse have been frequently described (Kaye *et al.*, 2004). In terms of personality traits the most common are the obsessive-compulsive personality traits (OCPD) and



borderline traits. Finally, early developmental disorders have been also associated with AN, such as ASD and attention deficit hyperactivity disorder (ADHD) (Wentz *et al.*, 2005).

Severe malnutrition and starvation lead to the physical and mental deterioration which makes AN one of the main causes of disability among young women (Flament *et al.*, 2001). Some of the problems associated with AN are cardiovascular and gastrointestinal problems, a compromised immune system, cognitive and brain dysfunctions, decrease of brain volume, muscle-skeletal complications such as weakness and loss of strength, osteopenia and osteoporosis. Most of these and other medical conditions recover after weight gain but osteoporosis (Misra and Klibanski, 2006) and reduced brain volume both appear to remain (see Katzman *et al.*, 1996, Katzman *et al.*, 1997, Wagner *et al.*, 2006b).

#### **1.2.2.2 *Bulimia Nervosa***

Etymologically, the term ‘bulimia’ (from the Greek ‘bous’ and ‘limos’) means either “an appetite as large as an ox or the ability to consume an ox” (Bisaga and Walsh, 2005, pp. 22) and allude to one of the main diagnostic characteristics of the disorder: the presence of binge eating.

Bulimia Nervosa became a recognised ED entity itself only in the late 20<sup>th</sup> century after the seminal paper of Gerald Russell in the UK, followed by its inclusion in the DSM-III. However, earlier descriptions of the syndrome standing independently from AN date back 1972 with the description of three cases by a Chilean psychiatrist Otto Dörr-Zegers (Vandereycken, 1994) and more systematically 1973 in Hilda Bruch’s work (Bruch, 1973). All these authors described BN as a normal weight syndrome characterised by regular engagement in hyperphagia and purging or other compensatory behaviours.

The DSM-IV criteria for BN are displayed in Table 1.2. The criteria emphasise the regular and recurrent presence of episodes of over-eating accompanied by inappropriate compensatory behaviours to prevent weight gain that usually follow an episode of binge. As in the case of AN, there are two sub-types of BN: *purging type* (PBN), which is characterised by the recurrent use of purging methods to prevent weight gain (e.g. self-induced vomiting, misuse of laxatives, diuretics or other medicines), and the *non-purging type* (NPBN) in which the individual does not

engage in purging behaviours and instead use behaviours such as fasting or excessive exercise to prevent weight gain.

In a recent review, Steiger and Bruce (2007) summarised the phenomenological variants present among people with bulimic spectrum disorders (including purging disorder (Keel, 2007) and BED), distinguishing three broad sub-phenotypes that express the high heterogeneity of the bulimic disorders: around one third correspond to the ‘dysregulated’ classical and more common description of individuals with BN; another third would be those ‘overregulated’ or ‘compulsive’ individuals; and finally, a group of BN individuals would be psychologically intact BN patients but with high trait of perfectionism.

**Table 1.2 Current diagnostic criteria for BN according DSM-IV (1994)**

---

Bulimia Nervosa
A. Recurrent episodes of binge eating. An episode of binge eating is characterised by both of the following: 1) eating, in a discrete period of time (e.g. within any two-hour period), an amount of food that is definitely larger than most people would eat during a similar period of time and under similar circumstances 2) a sense of lack of control over eating during the episode (e.g. a feeling that one cannot stop eating or control what or how much one is eating)
B. Recurrent inappropriate compensatory behaviour in order to prevent weight gain, such as self-induce vomiting; misuse laxatives, diuretics, enemas, or other medications; fasting; or excessive exercise
C. The binge eating and inappropriate compensatory behaviours both occur, on average, at least twice a week for three months
D. Self-evaluation is unduly influenced by body shape and weight
E. The disturbance does not occur exclusively during episodes of Anorexia Nervosa

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Bulimia Nervosa is commonly associated with co-morbid psychiatric and medical complications. Within Axis I disorders, the most common concurrent conditions for BN are mood disorders, particularly major depression and anxiety disorders (Herzog *et al.*, 1992, Kaye *et al.*, 2004). ADHD, OCD and impulsive behaviours, are also common (Biederman *et al.*, 2007, Kaye *et al.*, 2004, Råstam, 1992, von Ranson *et al.*, 1999, Wentz *et al.*, 2005, Wonderlich *et al.*, 2005). Binge purging BN (BPBN) has been also associated with addictive behaviours (Gadalla and

Piran, 2007). With regards to Axis II disorder, OCPD and avoidant personality disorders have been found to be present in BN. Also, an association with cluster B e.g. borderline personality is often reported (Anderluh *et al.*, 2003, Halmi *et al.*, 2005a, Lilienfeld *et al.*, 2006, O'Brien and Vincent, 2003, Zeeck *et al.*, 2007).

There are a number of medical conditions associated with purging behaviours, such as risk of electrolytic imbalance, heart failure, oesophageal damage, abnormal salivary glands and problems with the teeth, gums and lips, etc. (Fairburn and Harrison, 2003).

### 1.2.3 Epidemiology of eating disorders : An overview

#### ***Anorexia Nervosa***

Anorexia nervosa affects mainly, but not only, young women, with more than 90% of cases corresponding to female population (Fairburn and Harrison, 2003). The prevalence rate is decreased in the older population (van Hoeken *et al.*, 2003). The onset of the illness is more frequent during adolescence. For example, the highest incidence rate (i.e. the number of new cases in the population in a period of a year) in primary care was found in women between 10 and 19 years old (34.6 x 100000), with two peaks at the age of 12 and 18.

The average lifetime prevalence rate of AN (i.e. the total number of cases in the population that have suffered the disorder) has been estimated to be around 0.3% for young females (Hoek, 2006, van Hoeken *et al.*, 2003). Although an increasing incidence rate has been reported during the second half of the 20<sup>th</sup> century (van Hoeken *et al.*, 2003), a relative stable trend has been observed in Europe since the 1970s (Hoek and van Hoeken, 2003, van Hoeken *et al.*, 2003). For instance, a recent report found an incidence rate of 4.7 x 100000 population in primary care during the year 2000, with a remarkable consistency over a period of six years (1994-2000) in women aged 10-39 years, supporting previous observation of stability in the incidence rates of AN (Currin *et al.*, 2005). As mentioned above, the incidence rate in females was found to be twelve fold higher than in males (8.6 and 0.7 per 100000 population for females and males, respectively).

Although mortality caused by AN is not common relative to the general population, mortality rates are the highest in comparison with deaths caused by other

psychiatric conditions (Striegel-Moore and Bulik, 2007). The crude mortality rate (i.e. the fraction of deaths within the study population) was estimated at 5.9% in a meta-analysis of 42 published studies and deaths were mainly due to eating disorder complications and suicide (Sullivan, 1995). The standardised mortality rate (the fraction of the observed mortality rate – crude mortality rate - compared to the expected mortality rate in the population of origin) was 9.6% in studies with 6 to 12 years follow-up and 3.7% in studies with 20 to 40 years follow-up (van Hoeken *et al.*, 2003).

### ***Bulimia Nervosa***

The onset of BN is usually in late adolescence. Similarly to the case of AN, young females (aged 10 to 19) have the highest incidence rate (estimated in 6.6 x 100000 population) (Keel and Mitchell, 1997). The average lifetime prevalence rate for BN in young females has been estimated at around 1% (van Hoeken *et al.*, 2003). The prevalence rate for males is about 0.1% (Hoek and van Hoeken, 2003).

In contrast to AN where there is a broad constancy over time since the 1970's, Currin *et al.* (2005) reported that the incidence rate for BN in primary care has been more fluctuating, with an overall increase in the incidence of BN since 1988 to 2000 but with a trend to decline after a peak reached in 1996. Most of this decline has been associated with the decrease in the incidence rate for females aged 20-39 years. It has been argued that a change in the use of primary care services linked to the accessibility of alternative interventions (e.g. eating disorders associations) and a decrease in symptom recognition may have influenced the decrease in the incidence rate in the second half of the 1990's. However, the incidence rate of BN was still very high in primary care during the year 2000, with a rate of 12.4 x 1000000 for females and 0.7x100000 population for males indicating a relative risk for females to males of 18:1.

The standardised mortality rate was estimated at 7.4% (95% CI 2.9-14.9) in studies with 5 to 11 years follow up from the detection of the illness and (Nielsen, 2001), although crude mortality rates were found to be below 0.5% (van Hoeken *et al.*, 2003).

Finally, in a recent publication, Hay and collaborators report an overall increase in the prevalence of eating disorders in a period of 10 years (1995-2005), particularly in EDNOS rather than BN or AN, with a specific increase of binge

eating, purging and strict dieting or fasting in both women and men using a two cross-sectional sequential community survey in South Australia (Hay *et al.*, 2008).

#### 1.2.4 Course of illness and lifetime diagnostic cross-over

Anorexia Nervosa and Bulimia Nervosa are chronic disorders and the course of the illness is highly variable.

On average, duration of illness for AN is 7 years (Beumont and Touyz, 2003) and residual symptomatology is common (Herzog *et al.*, 1999, Lowe *et al.*, 2001). Rates of relapse are high even after full remission of symptoms in hospital (Carter *et al.*, 2004). In a systematic review of outcomes of AN in the 20th century, Steinhausen reports that overall only around a half of patients reach full recovery, one-third improve with residual features of the illness and 20% have a chronic illness over time (Steinhausen, 2002). Outcomes varied considerably according to three factors: duration of follow-up, age of onset and time period of study (e.g. studies between 1950-1979, 1980-1989 and 1990-1999). Better outcomes were associated with longer follow-up and younger age of onset, whereas bulimia, binges, abuse of purging methods, chronicity of illness and OCD, were linked to poor outcomes. Similar results in terms of rates of recovery were found by Lowe *et al.* (2001) in a prospective 21 year follow-up study. However, in the latter study, poor prognosis was associated with lower BMI and high rate of social and psychological problems.

The scenario is quite similar for BN in sufferers who have received treatment; around a half recover, 20 % persist with a full syndrome and 30% follow a course marked with relapse and remissions or would be categorised as EDNOS (Hsu, 1995). However, many sufferers of BN never seek help (Fairburn and Harrison, 2003). A less favourable prognosis in BN is associated with the incidence of impulsive behaviours (Fichter and Quadflieg, 2004), duration of illness and a history of substance abuse (Keel *et al.*, 1999).

Overall, full recovery from an ED seems difficult to achieve with less than a third of the diagnosed cases falling in a 'no ED' category after 30 months from the detection (Milos *et al.*, 2005). However, rates of remission seem to improve with time. Generally speaking, better prognosis is found in ED cases without purging

behaviours than those who engage in them (e.g. Milos *et al.*, 2005, Steinhausen, 2002).

An interesting phenomenon during the course of illness is how the phenotype is unstable over time (Anderluh *et al.*, 2008, Fichter and Quadflieg, 2007, Milos *et al.*, 2005, Treasure *et al.*, 2006). During the course of the illness, only one third of the patients retained their original diagnosis in longitudinal studies considering migrations between ED diagnosis and remissions (Fichter and Quadflieg, 2007, Milos *et al.*, 2005). AN was the most stable ED diagnosis followed by BN and the EDNOS. The least stable diagnosis is BED. Migration between ED diagnoses occurring in over half of cases (Anderluh *et al.*, 2008, Bulik *et al.*, 1997, Milos *et al.*, 2005). A large proportion of AN cases (up to around 50%) evolve into BN during the course of the illness (Bulik *et al.*, 1997, Strober *et al.*, 1997, Tozzi *et al.*, 2005). The crossover from BN to AN binge-purge subtype is less common but still occurs in up to one third of the cases and to restricting AN is very rare (Anderluh *et al.*, 2008, Fichter and Quadflieg, 2007, Fichter and Quadflieg, 2004, Tozzi *et al.*, 2005).

#### 1.2.5 Risk, aetiological and maintenance factors

##### ***1.2.5.1 An overview of risk factors to the development of eating disorders***

There is no single cause that predisposes individuals to develop an ED. Multiple risk and vulnerability factors; both biological (genetic and early developmental trauma) and environmental variables interact in the development of these illnesses (Collier and Treasure, 2004, Connan *et al.*, 2003, Fairburn *et al.*, 1999b).

The most comprehensive reviews of risk factors which have been defined as “variables that has been shown to prospectively predict some subsequent pathological outcome” (Stice, 2002, pp. 825), have found shared and distinctive variables of risk for AN and BN (Jacobi *et al.*, 2004, Stice, 2002, Striegel-Moore and Bulik, 2007).

Gender is the most potent risk factor for ED (Striegel-Moore and Bulik, 2007). Increasing evidence from genetic studies (family, twin, molecular and linkage studies) have highlighted the high heritability of ED that ranges from 48% to 76% in AN and 50% to 83% in BN studies. Candidate gene and association studies

suggest that networks involving dopamine, serotonergic systems, and brain derived neurotrophic factors may be of relevance (Bulik *et al.*, 2007b, Striegel-Moore and Bulik, 2007).

In a review which synthesised risk factor data in the form of a meta-analysis, perfectionism, body dissatisfaction, negative affect, impulsivity, use of substances and perceived perception of pressure to be thin were key factors for the genesis of ED (Stice, 2002). The thin-ideal internalisation and pressure for thinness may potentiate other risk factors. Specific risk variables for bulimic pathology include the direct modelling of body image and eating disturbance in family and close friends. Interestingly, dieting itself was not a risk factor but attenuated tendencies to over-eat. Finally, this revision highlighted the importance of social support as a protective factor to the development of an ED.

Jacobi *et al.* (2004) analysed the literature on cross-sectional and longitudinal studies in risk factors for ED. Common risk factors were female gender, ethnicity (except Asian), genetic factors (high heritability), early childhood problems related to feeding and gastrointestinal problems, childhood adversities (such as sexual and physical negative experiences), adolescence, negative self-evaluation or low self-esteem, psychiatric morbidity (mood and anxiety disorders) and as main risk factors, weight and shape concerns, body dissatisfaction and dieting. Specific risk variables for BN were pregnancy complications, childhood obesity, parental problems (e.g. alcohol), other family environmental factors (e.g. high criticism), negative self-evaluation. In the case of AN, specific risk factors were pregnancy and birth complications, high perfectionism and negative self-evaluation.

#### ***1.2.5.2 A neurodevelopmental aetiological model for eating disorders***

Many of the aforementioned risk factors for eating disorders are non-specific to ED and are common to other forms of psychopathology. Also, none of them are causal factors i.e. the presence of one or more risk factors in one individual does not determine the development of the illness. Many researchers and clinicians have tried to understand why only certain individuals presenting similar risk factors developed the illness. Several aetiological models have been proposed.

One model is that AN is a neurodevelopmental disorder in which an interaction between genes and the environment (early life and pubertal experiences),

sets the basis for developing the disorder during adolescence (Connan *et al.*, 2003, Favaro *et al.*, 2006, Gillberg *et al.*, 1994b, Southgate *et al.*, 2005a, Wentz *et al.*, 2000). Some of the arguments that support this model include the presence of dysdiachokinesis, a soft neurological sign, which suggests an inherent underlying immaturity or other abnormality of the central nervous system (Gillberg *et al.*, 1994b, Wentz *et al.*, 2000). Also, a high prevalence of developmental disorders in childhood are found in people who later on in life develop AN (Wentz *et al.*, 2000). Developmental events early in life even before birth may result in anomalies in brain development that are associated to the disorder (Favaro *et al.*, 2006).

In a model proposed by Connan *et al.* (Connan *et al.*, 2003) and later updated by Southgate *et al.* (Southgate *et al.*, 2005a), the development of an eating disorder is hypothesised to represent a maladaptative stress response in genetically vulnerable individuals (Connan *et al.*, 2003) The possible individual vulnerabilities might consist of anomalies in the development of the hypothalamic-pituitary-adrenal axis, poor coping strategies and vulnerabilities in the neural template. A chronic mode of stress response might ensue low self-esteem and poor emotional coping strategies. The disorder itself interrupts the normal maturational progress in the brain development in a critical period. Such a dysregulation in social, emotional and cognitive processing might contribute to the development of eating and other disorders i.e. mood and anxiety disorders (Nelson *et al.*, 2005).

In the case of BN, the above described neurodevelopmental model is also relevant as both disorders share the general aetiological explanation based on gene-environment interaction, a maladaptative stress response, poor coping mechanisms and the involvement of the serotonin system. However, background appetite factors often differ (Kaye, 2008, Steiger and Bruce, 2007).

One hypothesis resulting from this model is that people with ED would show anomalies in the neural template which may manifest as disturbances in informational processing, such as the rigidity and other OCDP traits seen in childhood that may be linked to difficulties in cognitive flexibility (set-shifting) and extreme attention to detail (Anderluh *et al.*, 2003, Southgate *et al.*, 2005a).



### 1.2.5.3 *Maintenance model for eating disorders*

Whereas the awareness of risk factors is highly valued in the area of prevention of ED in general and in risk factor populations, maintenance factors i.e. “factors that predict symptom persistence over time versus remission among initially symptomatic individuals” (Stice, 2002, pp. 826) are key in the understanding of how individuals get trapped in the illness and therefore are informative and of utmost interest in the development of treatment for ED (Shafran and de Silva, 2003, Stice, 2002). In his systematic review, Stice noted the importance of perfectionism as a maintaining factor for ED pathology in general and thin ideal internalisation, body dissatisfaction and negative affect for bulimic pathology.

Few pure maintenance models have been developed for ED (Fairburn *et al.*, 1986, Fairburn *et al.*, 2003, Fairburn *et al.*, 1999a). Recently, Schmidt and Treasure (2006) have described the new *Maudsley model of maintenance for AN* where they have collected empirical evidence. This model combines the evidence for both *intra* and *inter*-personal elements which help to maintain the illness and may impact on treatment outcomes. The model proposes two disposition factors that *precede* the onset of AN: (1) Obsessive-compulsive personality traits manifested in rigidity and perfectionism, that in turn predispose to cognitive and behavioural traits such as dichotomous thinking, attention to detail and fear of mistakes, etc., and (2) High anxiety and avoidance of intense emotions and intimate relationships that might provoke those emotions. The model also includes two factors that are *consequences* of severe starvation: (3) Reactions by close others with high expressed emotion (overprotection and criticism) and other behaviours that inadvertently enable the AN behaviours, such as tolerance or accommodation of symptoms, and (4) Biological and psychological changes which are perceived to be positive by the individual and serve as a base for pro-anorexia beliefs.

This model could be extended for the understanding of other ED, such as BN, particularly as this group share the compulsive phenotype of these disorders (Treasure, personal communication).

### 1.2.6 A note about treatment and treatment outcomes<sup>1</sup>

Recently, a number of reviews have addressed treatment outcomes in ED (Agras *et al.*, 2004, Bulik *et al.*, 2007a, Shapiro *et al.*, 2007). The evidence in favour of effective treatment is still limited, especially for AN (NICE, 2004).

Relative good outcomes have been reported in BN with both psychological and pharmacotherapy treatments. Cognitive behavioural therapy (CBT) is recommended as the treatment of choice by the National Institute of Clinical Excellence in the UK (NICE, 2004). CBT should aim to interrupt the bulimic cycle and address cognitive patterns which maintain the illness. Most treatment occurs in outpatient settings and self-help methodologies may be offered as adjuncts to traditional treatment (see systematic review: Perkins *et al.*, 2006).

The scenario, however, is less encouraging for treatments for AN. It has been argued that this group of patients is one of the most difficult groups to treat (Halmi *et al.*, 2005b). Some of these reasons for this include patients' ambivalence towards change, the need to interrupt psychological treatment due to medical conditions, the positive and valued function that AN has in patients' lives, the denial of the illness and its consequences, co-morbidity and personality traits like perfectionism (Bulik *et al.*, 2007a, Crane *et al.*, 2007, Halmi *et al.*, 2005b, Schmidt and Treasure, 2006). Overall, a poor outcome has been found in treatment trials for AN (Berkman *et al.*, 2007). A multifaceted form of treatment is necessary for AN, including both psychological elements alongside medical and nutritional monitoring and guidance.

Further research is needed to clarify what are the factors that help to improve outcomes. It is difficult to find differences in symptomatic outcomes between forms of treatments, in part because clinics and families often violate the protocols to maintain safety i.e. someone with very low weight will be admitted over the course of a trial. Other outcomes such as economic variables may be of interest (e.g. Byford *et al.*, 2007, Gowers *et al.*, 2007).

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<sup>1</sup> Treatment will be discussed later in Chapter 8 and 9.

### 1.2.7 Conclusion

Eating Disorders are complex psychiatric conditions that affect mainly young females and produce high disability and burden in sufferers and their families. In the aetiology and maintenance of these disorders complex interactions between biological, genetic and psychosocial factors are involved. Treatment is so far unsatisfactory with better outcomes for BN than for AN. However, in both syndromes, barely half of all sufferers reach full recovery. Therefore, sufferers have a persisting and devastating course of illness. Treatments have largely focused on remediation of the overt ED phenotype i.e. weight and shape concerns. A better understanding of the aetiology and maintenance of ED may open up new routes to developing more successful treatments. For example, treatments that target illness processes (e.g. maintenance factors) may have greater efficacy. These would need to address those sometimes underlying variables that underpin traits that make the illness difficult to overcome (Schmidt and Treasure, 2006).

In what follows below, we address the concept of endophenotypes in psychiatry. We propose that looking at the intermediate phenotypes would be a useful approach to find new effective ways of treating ED. We focus specifically in cognitive traits that might underpin obsessive-compulsive behaviours that maintain the illness and link with autistic spectrum disorders (ASD).

## **1.3 The Study of the Endophenotypes in Eating Disorders**

### 1.3.1 Endophenotypes in psychiatry

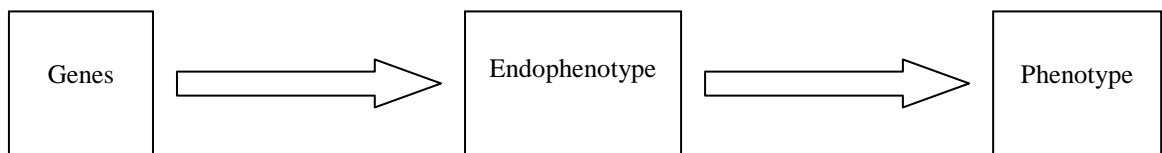
Psychiatric disorders are complex disorders in both their aetiology and phenotypic manifestations. The variability in the phenotype can make research into fixed markers difficult. An alternative solution is to focus on the study of persisting underlying traits of the illness (Gottesman and Gould, 2003).

The identification of putative *endophenotypes* is a way of deconstructing complex psychiatric disorder in order to understand the diseases process (Gottesman and Gould, 2003).

The origins of the endophenotype concept derive from work in 1966 in the study of the evolution and biology of insects. The internal and microscopic

phenotype was defined as an endophenotype opposed to the obvious external exophenotype. It was later adapted by Irving Gottesman and Todd Gould for the study of psychiatric conditions such as schizophrenia in 1973 (Gottesman and Gould, 2003). Increasing interest in this concept is reflected in its exponential use in the scientific literature in the last decade. A PubMed search showed only 9 entries before 2000, 113 in before 2004 and 407 in May 2008.

As defined by Gottesman & Gould (2003), *endophenotypes* are objectively measurable intermediate constructs that lie on the causal pathway between genes and the illness indexing an underlying vulnerability to a disorder or behavioural trait (see Figure 1.1). Seven categories of possible candidates for endophenotypes have been identified: anatomical (e.g. ventricular enlargement in schizophrenia), developmental (e.g. age at first word in autism), electrophysiological (e.g. EEG coherence in alcoholism), metabolic (e.g. changes in the HPA axis), sensory (e.g. olfactory sensitivity in schizophrenia) or psychological/cognitive (e.g. response inhibition in ADHD) (Flint and Munafò, 2007).



**Figure 1.1 Endophenotype on disease pathway (Walters and Owen, 2007)**

In order for any trait to fulfil the criteria for an endophenotype it must (1) be associated with illness in the population (2) be state-independent i.e. manifest in the individual even when the illness is not active, (3) be present at higher level in unaffected relatives than in general population, (4) be heritable, and (5) be linked with disorder in families (Gottesman and Gould, 2003). The criterion of state-independence was later modified in order to consider epigenetic (i.e. changes in gene-expression influenced by environmental factors that do not involve a change in the underlying DNA) and developmental factors so the endophenotype can be noticeable only at a certain age or in response to a laboratory-based assessment of a

challenge (e.g. glucose tolerance test) (Braff *et al.*, 2007, Hasler *et al.*, 2006). Recent refinements to the endophenotype concept include the requirement of being linked to the causal process of the illness, being able to probabilistically predict the disorder, and being closer to the site of the primary causal agent than the diagnostic categories (Flint and Munafò, 2007). All these criteria are difficult and highly costly to demonstrate in the field of psychiatry.

There are a number of concepts that has been used interchangeably to refer the term 'endophenotype' such as 'intermediate phenotype', 'biological markers', 'subclinical traits', 'vulnerability marker' etc. However, Gottesman differentiated biological markers from endophenotypes on the basis that an endophenotype must have genetic underpinnings (Gottesman and Gould, 2003).

The endophenotype approach has been incorporated into the study of psychiatric disorders such as schizophrenia (e.g. Braff *et al.*, 2007, Braff and Light, 2005, Calkins *et al.*, 2007), ADHD (e.g. Doyle *et al.*, 2005), Alzheimer's (e.g. Neugroschl and Davis, 2002), anxiety and mood disorders (e.g. Hasler *et al.*, 2006, Lenox *et al.*, 2002, Niculescu and Akiskal, 2001), autism (e.g. Bölte and Poustka, 2006) and alcoholism (Flint and Munafò, 2007). Although the use of an endophenotype approach in psychiatry is promising, advantages related to the main purpose of the endophenotype study in the detection of more simpler genetic architecture to disorders that the disease to which they are related have not yet been demonstrated (Flint and Munafò, 2007, Walters and Owen, 2007).

In the recent years the 'endophenotype' concept has gained increasing popularity in the field of ED and has been discussed in several reviews (e.g. Bulik *et al.*, 2007b, Gillberg *et al.*, 2007, Holliday *et al.*, 2005, Hudson and Poper, 2007, Steiger and Bruce, 2007, Treasure, 2007, Treasure *et al.*, 2007a, Zucker *et al.*, 2007).

In the study of ED, an endophenotype approach is particularly useful especially in the context of the multifaceted and fluctuating form of ED phenotypes (Fichter and Quadflieg, 2007, Milos *et al.*, 2005). This approach would not only help in the genetic dissection of the ED and increase the power and consistency of genetic studies, but it may allow for the identification of transdiagnostic risk factors as well as specific factors (Collier and Treasure, 2004).

### 1.3.2 Endophenotype candidates in eating disorders

Some candidate endophenotypes relevant to ED include enduring and underlying traits such as reward sensitivity, impulsivity, compulsivity, hyperactivity, neuroendocrine biomarkers (e.g. serotonin function), and neuropsychological measures (Collier and Treasure, 2004, Treasure, 2007).

Some other potential endophenotypic candidates for those which there is insufficient evidence so far or/and studies which need replication for inconsistent data are: attention (Lauer *et al.*, 1999) and cognitive/behavioural disinhibition (Bruce *et al.*, 2003, Kaye *et al.*, 1995, Southgate *et al.*, 2007, Toner *et al.*, 1987) for the bulimic spectrum of disorders (Steiger and Bruce, 2007), and anomalies in fear conditioning (Strober, 2004), dysregulation in reward systems (Treasure *et al.*, 2007a, Wagner *et al.*, 2007), atypical physiological response to stress (Connan *et al.*, 2003, Tchanturia *et al.*, 2007b, Treasure *et al.*, 2007a, Zonneville-Bender *et al.*, 2005), problems in social cognition (Zucker *et al.*, 2007), perfectionism and other OCPD traits in AN (Treasure *et al.*, 2007a, Wade *et al.*, 2008).

To date, only two published studies have identified potential endophenotype candidates for the ED population which fulfil at least two of the necessary criteria: impaired set-shifting in AN (Holliday *et al.*, 2005) and reduced brain serotonin (5HT) transporter activity in BN (Steiger *et al.*, 2006). Both potential candidates are not specific to ED (Steiger and Bruce, 2007, Treasure, 2007).

Another small study that examined the hypothesis of serotonin transporter (SERT) binding as an endophenotype for BN did not find enough evidence to support the hypothesis (Koskela *et al.*, 2007). The study may need replication with a larger sample size.

#### ***1.3.2.1 Rigidity/OCPD as the phenotype and difficulties in set-shifting as a potential neuropsychological endophenotype for eating disorders***

In the cognitive literature of ED, Lena *et al.* (2004) proposed that some of the cognitive traits apparent in the acute phase of an ED are predisposing factors in that they may be present in childhood in many patients and that they may also be perpetuating factors determining the fluctuating course of the illness. In support of this argument is the finding that cognitive abnormalities seen in the active state of the

disorder do not improve after refeeding and weight recovery e.g. (Green *et al.*, 1996, Kingston *et al.*, 1996, Southgate *et al.*, 2006, Szmukler *et al.*, 1992).

People suffering from AN typically exhibit obsessive-compulsive personality traits such as rigidity, perfectionism and attention to detail (Anderluh *et al.*, 2003). Treasure (2007) proposed perfectionism and cognitive ‘rigidity’, may be underpinned by poor set-shifting and detail focused thinking style.

Set-shifting is one of the main aspects of executive functioning and refers to the ability to switch or alternate between tasks, operation or mental sets (Miyake *et al.*, 2000). Impaired set-shifting, manifested in poor and delayed set-shifting and cognitive rigidity in neuropsychological tests, is the only cognitive trait so far that has been examined under the light of the endophenotype approach and has demonstrated enough evidence to be named as a potential endophenotype for AN. The evidence to support this argument is based on studies that have found that difficulties in set-shifting are associated with the illness in its acute form in AN (Fassino *et al.*, 2002, Tchanturia *et al.*, 2004a), do not improve with weight gain, although effects seem to reduce (Roberts *et al.*, 2007, Tchanturia *et al.*, 2004c), remain as a trait in well recovered individuals (Tchanturia *et al.*, 2004c), and they have been found in higher proportion in non-affected relatives of people with AN relative to a control group (Holliday *et al.*, 2005). All above represent evidence in favour to claim that set-shifting may be a biomarker for AN.

Moreover, impaired set-shifting has been found across ED categories and states of illness in a systematic review of 15 studies using several paradigms assessing aspects of cognitive flexibility i.e. perceptual and mental shifting (Roberts *et al.*, 2007). The fact that deficient performance in set-shifting task has been described in BN as well as in AN suggests that it could be an endophenotype for general ED. The meta-analytic review found that people with ED perform generally poorer than healthy controls in measures of set-shifting with pooled effect sizes that varied from small in the Trail Making Test-B, to medium for Wisconsin Card Sort Test and CatBat Test, to large for the perceptual shifting test of Haptic Illusion. However, reduced effect sizes are found in recovery. Replication of these studies and further research might be needed to determine which aspects of set-shifting fulfil the criteria for an endophenotype and which measures are the most informative and reliable since not all the dimensions of this concept have shown equal impairment

across the aforementioned studies and there are some inconsistent results according a meta-analytical review recently published (Roberts *et al.*, 2007)

Impaired set-shifting has been found in other psychiatric disorders somewhat linked to ED, like autistic spectrum disorders (ASD) (e.g. Hughes *et al.*, 1997, Hughes *et al.*, 1994, Ozonoff *et al.*, 1991) and obsessive-compulsive disorders (OCD) (e.g. Bannon *et al.*, 2006, Chamberlain *et al.*, 2006, Hymas *et al.*, 1991, Veale *et al.*, 1996, Watkins *et al.*, 2005) and has also been associated with the endophenotype of these disorders (e.g. Chamberlain *et al.*, 2007, Delorme *et al.*, 2007, Hughes *et al.*, 1997, Hughes *et al.*, 1999).

More research is needed to systematically examine potential endophenotype candidates in the field of ED and to investigate whether ED endophenotypes can help the development of a model of illness processes and inform treatment interventions.

Ongoing research in our group (Roberts, personal communication) has taken a systematic approach to thoroughly address the endophenotype criteria for set-shifting impairment and is also looking at the heritability of this trait for AN and BN.

## **1.4 Central Coherence as an Candidate Endophenotype**

### **1.4.1 Central Coherence: Definition and development of the concept**

The study of cognitive styles has a long history in the field of normal psychology, education and neuropsychology.

Witkin *et al.* (1950, 1971) defined cognitive styles as a characteristic mode of functioning which an individuals show in their perceptual and intellectual (cognitive) abilities. A cognitive style manifests therefore beyond the area of intellectual ability affecting the broader dimension of personal functioning.

This definition has brought relevant consequences in cognitive and personality research and an increasing interest to identify the most accurate descriptions of cognitive styles in general population. For example, Riding and Cheema, from the educational field, (1991) found more than 30 labels for cognitive/learning style in the literature.

The study of the core characteristics of cognitive styles has surpassed the boundaries of normal psychology to apply to the study of psychiatric disorders.



In the field of autism research, Dr. Amita Shah and Uta Frith took the study of the particular way of thinking of this group further. They noticed that people with autism presented relative impairments as well as advantages in their cognitive functioning (Shah and Frith, 1993). Interestingly, they observed that those with autism excelled in performance on tasks such as Block Design Test (see description in Chapter 2). They hypothesised that this extraordinary phenomenon may be explained by a particularity of the cognitive style in autism that manifests as the opposite tendency than that observed in typically developing adults. Uta Frith (1989) pointed out that the natural cognitive styles of most people in adult life is characterised by a tendency to integrate large amounts of incoming information into context, gestalt and meaning. The opposite thinking style, so called *weak central coherence*, was therefore utilised to refer to “a processing bias for featural and local information, and relative failure to extract gist or ‘see the big picture’ in everyday life” (Happé and Frith, 2006, pp. 6). Years of research in the area have suggested that this cognitive style is the predominant processing style among individuals with ASD (Frith, 1989, Happé and Frith, 2006, Shah and Frith, 1983, Shah and Frith, 1993). This mirrors one of the main diagnostic characteristics of the syndrome present in its original description as the obsessive ‘preservation of the sameness’ (Kanner and Eisenberg, 1956) now translated as a ‘persistent preoccupation with parts of objects’ (APA, 1994).

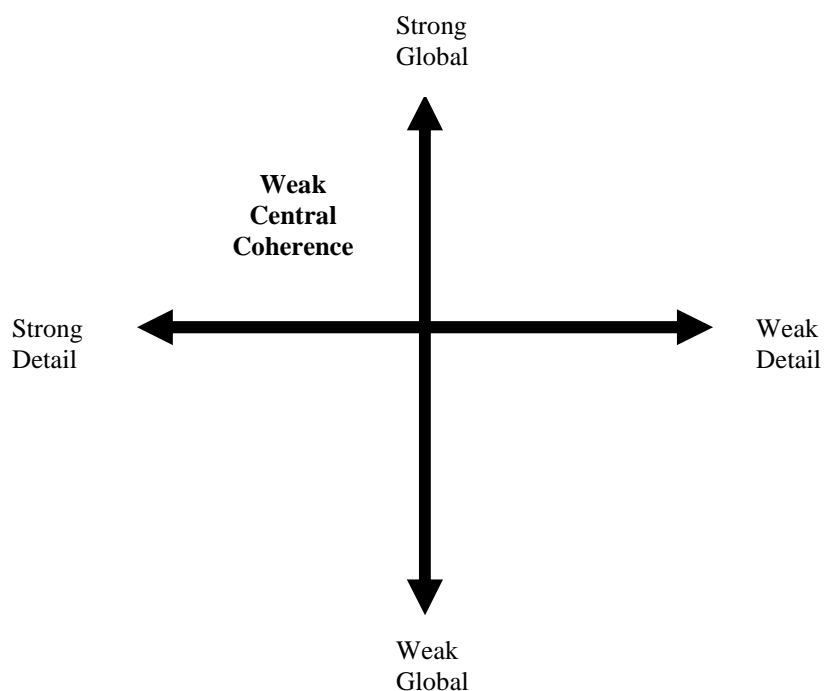
The evidence supporting the weak central coherence account in ASD, was collated in a comprehensive literature review by Frith and Happé (2006). This review found around 60 studies relevant to the weak coherence account in this population (see section 1.4.4 for a summary of results).

The authors concluded that the original concept of Frith in 1989, which claimed weak central coherence as a core deficit in people with ASD, needed to be modified in the light of the new evidence. Three main characteristics of this cognitive style were then proposed: weak central coherence (1) may imply superiority in detail-focused processing and a relative deficit in global processing would be a secondary outcome to the local predominance, (2) could be considered a bias more than a deficit that could be surpassed when the subject is explicitly required to employ global processing, and (3) instead of being the core causal explanation of other cognitive characteristics in ASD, weak central coherence would be one of many impairments in ASD, such as social cognition problems.

This more positive view of weak central coherence influenced greatly the recent research in ASD. Indeed, in a more recent review Happé and Booth (2008) revisited the concept of weak central coherence emphasising the two aspects of the weak central coherence concept: it would require both a **superiority in detail-focused** processing and a **deficit in global processing**. The latter, as noted by the authors, has been somewhat neglected in the latest reports of ASD. A side outcome of this revision of the concept is that the idea of central coherence as a continuum is questioned and instead a two-dimension concept is argued. In other words, an individual's cognitive style could be described based on the intersection of two axes i.e. detail and global processing with four resulting quadrants (see Figure 1.2).

This conceptualisation fits better with the evidence from developmental studies that have established independent trajectories of local and global processing, although the primacy of one over the other has not been clarified (Booth, 2006). What seems clear is that the balance between global and local processing increases with the age in typically developed individuals (Happé and Booth, 2008, Witkin *et al.*, 1971) and there is some evidence that efficient local processing in the visual perceptual and verbal domains is reached early in life, whereas efficient global processing continues to improve until the age of 8 (Brainerd and Gordon, 1994, Porporino *et al.*, 2004). However, it has been argued that whereas in typically developed individuals global and local processing are more independent and usually positively correlated, a trade-off relationship is more characteristic for individuals with ASD (Booth, 2006).

Finally, some others have emphasised the role of executive functions that may interact with local and global strategies aiding in their more efficient use. For example, it might be possible that the development of attentional or set-shifting strategies may help the individual's response adapt to external demands (Happé and Booth, 2008).



**Figure 1.2 Dimensional approach to weak central coherence account**

Although the concept of central coherence is relatively new and has been developed within the context of the study of ASD, other theoretical and experimental frameworks described before make reference to the same underlying concept (Riding, 2000). For example, Field Dependence-Independence (Witkin *et al.*, 1971), Levelling-Sharpening (Klein, 1954) and Impulsivity-Reflectivity (Kagan *et al.*, 1964) would fit relatively well with the central coherence conceptualization.

In the study of psychiatric disorders, and in ASD specifically, there are also a variety of accounts using terms that could be understood as alluding to aspects of the central coherence account, although an exact concordance between these terms has not yet been established. Some of these labels refer to ways of processing information that are characterised by a bias towards detail or difficulties in global processing in dichotomic categories such as concrete/abstract thinking, analytical/global processing, narrow/broad, part/whole, featural or local/ integrated or holistic, focussing/scanning, local/global precedence, perceptual/conceptual memory, etc. Also, some alternative accounts to weak coherence applied to ASD research have focused on only one, positive dimension of the detail/global intersection, such as enhanced perceptual functioning (Mottron *et al.*, 2006) or the

hypersystemizing theory (Baron-Cohen *et al.*, 2003). Also Plaisted's hypothesis of enhanced discrimination and reduced generalisation focused on superior visual search evidence rather than reduced integrative functions (Plaisted *et al.*, 1998). For a revision of alternative accounts to weak central coherence, see Happé and Frith (2006) and Happé and Booth (2008).

Finally, it is worth mentioning that even though central coherence has been mainly explored in people with ASD, there is some evidence for a local processing bias in schizophrenia, Williams Syndrome, anxiety/depression and right hemisphere damage. However, there is no clear answer to the question of specificity of weak coherence yet, as no comparison with ASD on the same tasks has been done (Happé and Frith, 2006).

#### 1.4.2 Biological mechanism underlying central coherence

Several theories have been advanced to explain weak central coherence in ASD.

One theory is that weak central coherence is associated with atypical function in specific regions in the brain (Happé and Frith, 2006). Indeed, anomalies in the right hemisphere might impair global processing (Fink *et al.*, 1997, Heinze *et al.*, 1998). Weak visual coherence has also been associated with impairments in the magnocellular visual pathway (Milne *et al.*, 2002, Spencer *et al.*, 2000) and with anomalies in the neural mechanisms needed to integrate local motion information in the dorsal visual pathway.

A second theory is that weak central coherence is caused by under-connectivity or by a lack of neural synchronization (Brock *et al.*, 2002, Frith, 2004, Just *et al.*, 2004). A pilot neuroimaging study using the Embedded Figures Test (EFT) found that people with autism and healthy controls shared some but not all patterns of activation. People with autism showed more activation in the right ventral occipitotemporal area, whereas healthy controls displayed increased activation in the right dorsolateral prefrontal and parietal regions. This suggests the employment of different strategies to solve the task; people with autism might use mental imagery and healthy controls use higher order visual perception and working memory.

Moreover, abnormal patterns of activation during the EFT were also found in parents of people with autism (Ring *et al.*, 1999).

More research is needed to be able to offer suitable explanations of mechanisms underlying global and local processing skills in both the general and psychiatric populations.

#### 1.4.3 Measures of coherence

Diverse paradigms have been used to address the use of local versus global cognitive strategies. Most, if not all, these tasks have been described in the field of ASD and only a few have been utilised in the study of other psychiatric illness.

In a general view, one can make categories based on assumptions of the main requirement of the tasks (local versus global tasks), levels of processing (high i.e. processing of meaning versus low i.e. perceptual), and predominant sensory domain (e.g. verbal/auditory, visual-spatial). It is important to mention that even though it is possible to classify tasks according the predominant ability required to successfully solve the task, most of the neuropsychological tasks combine the demands of local and global information processing. Therefore it is hard to identify whether the performance pattern displayed by individuals with ASD reflects strong local processing, weak global processing, or both (Booth, 2006, Happé and Booth, 2008). However, efforts for separating both dimensions of the weak coherence have been made through the development of specific tasks like the Fragmented Pictures to tap global, integrative abilities (Snodgrass *et al.*, 1987), certain variables measured within a tasks such as process measures in drawing tasks (Booth, 2006, Booth *et al.*, 2003), or the conjoined use of a variety of tasks tapping local and global processing whose analysis allow for discriminating better the underling processing account for example the use of some drawing tasks (Motttron *et al.*, 2003).

Also, some of tasks have been defined as open-ended tasks in which the assumption is that the individual cognitive style may be more freely displayed, as there is no a requirement of advantage in using either local or global skills (e.g. the Rey-Osterrieth Complex Figure). Finally, there are some tasks that have been designed to manipulate the local versus global processing requirements (e.g. modified hierarchical figure). Table 1.3 shows some of the measures of central

coherence used in the literature in an effort to separate them by domain and level of processing.

Processing Preference \ Domain	Visual-Spatial	Verbal/Auditory
Low perceptual level	Embedded Figures Tasks Block Design Task Impossible Figures Hierarchical figures (Navon) Illusion Task Motion Coherence Task Dot counting in canonical vs. distributed arrays Object integration test Modified Hoper Visual Organisation Test Visual search task	Phoneme Segmentation Chord Segmentation Chord Sequence Task Pitch Identification Pitch Memory Same-different judgements of melodies
High semantic level	Drawing tasks (Rey-Osterrrieth Figure, Pram Task) Faces tasks Picture Recognition Task Fragmented Pictures Scenic Test	Homograph Reading Task Sentences Completion Task Story Memory Task Gap test Ambiguous Sentence test

**Table 1.3 Measures of Central Coherence**

#### 1.4.4 Central coherence in autism spectrum disorders (ASD): An overview

Under the current understanding, a diagnosis of autism requires the co-occurrence of a behavioural triad consisting of the restricted and repetitive behaviour or obsessive interests, impaired social interaction, and impaired communication form the bases for its clinical diagnosis (Baron-Cohen, 2004, Happé *et al.*, 2006). These traits are also shared with Asperger’s syndrome, a subgroup of the autistic spectrum, and the difference between these diagnostic categories is that the latter syndrome does not present a delay in language development and presents normal or above

normal intellectual quotient (IQ), whereas in autism IQ may be lower than normal (Baron-Cohen, 2004). The DSM-IV criteria for autistic disorder includes a preoccupation with parts rather than wholes of objects (APA, 1994) a characteristic that might relate with the weak central coherence hypothesis (Happé and Frith, 2006).

Positive, conflicting and even negative findings have been reported with regards the weak coherence hypothesis in this group. However, the overall analysis indicate that there is stronger evidence in favour of superior local processing however there is less certainty as to whether this superiority in local processing is at the expense of global processing (central coherence).

For example, superior local processing was demonstrated in the visual-spatial domain with a very efficient processing of unconnected stimuli among individuals suffering from ASD demonstrated in tasks such as the Embedded Figures Test (Burnette *et al.*, 2005, Jolliffe and Baron-Cohen, 1997), another visual search task (Plaisted *et al.*, 1998), and Block Design Task (Happé, 1994, Shah and Frith, 1993), and in the verbal domain in several studies of musical perception (e.g. Heaton, 2003, Heaton *et al.*, 1998, Mottron *et al.*, 2000).

On the other hand, individuals with ASD have shown impairments in some tasks which involve global processing strategies. For example, they underperform on tasks measuring the perception of coherence motion (Bertone *et al.*, 2003, Milne *et al.*, 2002), have reduced gestalt grouping (Brosnan *et al.*, 2004), and abnormal face processing centred on detail (e.g. Hobson *et al.*, 1988). In the verbal domain reduced sensitivity to context in pronouncing homographs have been more consistently found (Burnette *et al.*, 2005, Happé, 1997, Hoy *et al.*, 2004, Jolliffe and Baron-Cohen, 1999) although some have argued that the deficits found in ASD are related more to low general ability than to weak coherence (Frith and Snowling, 1983, Hoy *et al.*, 2004).

Conflicting results have been reported with regards to the accurate identification of visual illusions (Happé, 1996, Hoy *et al.*, 2004, Ropar and Mitchell, 1999, Ropar and Mitchell, 2001), normal versus local advantage in Navon Hierarchical Figures (Mottron *et al.*, 1999, Plaisted *et al.*, 1999). Even though advantageous Block Design and EFT performance has been reported and replicated, some studies have found no difference between ASD and healthy controls on this task (e.g. Burnette *et al.*, 2005, Kaland *et al.*, 2007).

In the most comprehensive study of global versus local processing that has been conducted in ASD, Booth (Booth, 2006) studied differences in coherence between typically developed, ASD and matched controls using 16 different tasks tapping local and global processing in visual-spatial and verbal domains at both low and high levels processing. Booth reached the following specific and highly informative conclusions:

- In low level visual-spatial coherence tasks such as Block Design, EFT, Impossible Figures, Navon Similarity Judgement Task, predictions of weak central coherence account were met with the exception of superior local processing in Block Design. In all the other tasks those with ASD demonstrated a bias towards detail in higher proportion than typically developed individuals. In the latter a stronger effect of age and intellectual ability was found e.g. better local skills were positively related to IQ and age.
- In low level auditory coherence tasks like Phoneme and Chord Segmentation Tasks, Pitch Identification and Chord Sequence Task, the relationship between IQ, age and performance were again found in the healthy group. The ASD group did not show superior ability to disembedding auditory stimuli.
- In the high level visual-spatial processing tasks, there was a developmental general effect; therefore older individuals performed better. However, there was no support for a local bias across tasks in ASD, although difficulties in global processing were evident.
- In high level verbal tasks, the ASD group, particularly those with high functioning (i.e. Aspergers) showed less proficient use of context according to the predictions of the weak central coherence hypothesis. Performance in the Homograph Reading Task (HRT) was related with IQ and in the healthy group was a clear age effect that interacted with performance across tasks.

In summary, this outstanding study has added relevant information to the overall conclusion of Happé and Frith review (2006). It showed consistent evidence to support the superiority of local processing in the ASD population in tasks tapping low level processing of visual coherence, but failed to find superior processing in verbal/auditory domain, previously described as typical in autism (e.g. Heaton, 2003, Heaton *et al.*, 1998) and in high level visual processing tasks. Interestingly, the study failed to replicate findings of some previous studies in Block Design. One of the



main contributions of this work was to use a number of tasks tapping global processing abilities providing stronger evidence in favour of weak global processing across domains in ASD population. Finally, it provided further evidence about developmental aspects of coherence, potential confounding variables in the performance of some of the tasks (e.g. IQ), and conceptual issues. For instance, typically developed individuals are able to reach good local processing not necessarily at the expense of global processing and are more able to adapt their processing style to the demands of the task. In ASD, both styles seem to be in a trade-off with good 'eye for detail' going with poor integration.

The weak central coherence account in ASD has been challenged due to the lack of replication of some of the findings and the possibility of alternative explanations to the deficit/advantages demonstrated on the tasks thought to measure the concept (Hoy *et al.*, 2004). It has been argued that part of the conflicting data may be explained by the different definitions of global and local abilities which have been used (Happé, 1999). It might be possible that contributions such as the revisiting of the concept of weak central coherence made by Happé and Booth (2008) will improve consensus in future research.

Also, as it has been mentioned before, performance on most of neuropsychological tasks may involve a number of functions that make it difficult to discriminate the exclusive role of local and global processing skills. For example, some authors have concluded that evidence supporting the weak coherence account could be explained as a result of impaired executive functions (e.g. Hala *et al.*, 2007). However, the two studies that have examined the association between central coherence and executive function have found unrelated outcomes, indicating that weak coherence is not a mere result of executive functions (Berger *et al.*, 2003, Booth *et al.*, 2003).

Studies combining tasks to measure weak and strong coherence but designed to discriminate these two dimensions need to be conducted in order to clarify this enigma.

#### 1.4.5 Central coherence as an endophenotype for ASD

Happé and Frith (2006) have proposed that weak central coherence may be part of the ‘broader phenotype’ of ASD. To date there is some evidence from studies comparing healthy relatives and healthy controls to support the hypothesis that weak central coherence may be a heritable characteristic. An early study found similar results using Block Design Test (BD) in siblings and parents of ASD in comparison with control pairs finding moderate effect sizes<sup>2</sup> in favour of the advantageous performance of ASD relatives, although these differences were not statistically significant (Smalley and Asarnov, 1990). Baron-Cohen *et al.* (1997) found faster times in EFT in parents of ASD probands with moderate effect sizes ranging from  $d$  0.55 for mothers and  $d$  0.72 for fathers. Finally, Happé, Briskman and Frith (2001) administered three of the tasks commonly used in the study of central coherence in ASD (i.e. Block Design, EFT and Sentence Completion tasks) to unaffected first degree family members of boys with ASD. They found that a high proportion of parents showed neuropsychological performance in line with the weak central coherence account. In fact, around 50% of fathers and 30% of mothers displayed detail-focused processing. These findings were supported by self-report measures (Briskman and Happé, 2001).

Some studies that have used non-healthy control groups have also found supporting data to the aforementioned hypothesis. For example, Bölte and Poustka (2006) found that parents of ASD subjects, irrespective of gender, performed better in the EFT and BD than their two comparison groups (parents of individuals with early onset of schizophrenia and mental retardation). Three other studies (Fombonne *et al.*, 1997, Piven and Palmer, 1997, Szatmari *et al.*, 1993) comparing parents and siblings or parents only in BD and/or Object Assembly (OA; that may indicate global processing abilities) found mostly no difference when comparing relatives of down-syndrome (DS) probands and in one case an added comparison group of parents of children with low birth weight. The only exception was a poorer performance of ASD parents in OA in a comparison with DS parents (Piven and Palmer, 1997).

According to Happé and Frith (2006), these findings may offer an explanation as to why there is an increased proportion of parents of ASD individuals linked to

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<sup>2</sup> For an explanation of effect sizes, please refer to the Analysis of the Data section in Chapter 2.

professions like engineering that are thought to require strong detail processing (Baron-Cohen and Hammer, 1997).

In sum, weak central coherence might be part of the endophenotype for ASD, since it was found to be related to inherited abilities (Briskman and Happé, 2001, Happé *et al.*, 2001). Further studies will be needed in order to determine if this trait fulfils the criteria for endophenotype mentioned above.

### **1.5 Why Consider Central Coherence as an Endophenotype Trait in People with Eating Disorders?**

As discussed in a previous section of this chapter (see section 1.2.5.2), it has been argued that AN could be a neurodevelopmental disorder (Connan *et al.*, 2003) in which anomalies in emotional, social and cognitive processing may be present (Zucker *et al.*, 2007). The neurodevelopmental hypothesis would explain some of the links found between people with AN and ASD, such as the high prevalence rate of ASD caseness within people diagnosed with AN and the possibility that at least a sub-group of people with AN display similarities in clinical characteristics (e.g. empathy disorders) and information processing style with people ASD (Gillberg *et al.*, 1995).

Our group have found complementary evidence supporting Gilberg's observations in relationship with the cognitive processing, where people with AN performed more efficiently in tasks requiring a good 'eye for detail' (Southgate *et al.*, 2007). These findings would fit well with the predictions made by the weak central coherence account. Interestingly, clinical observations additionally support the extreme attention to detail and difficulties to integrate information into context beyond the laboratory settings (Davies and Tchanturia, 2005).

Finally, both AN and ASD are closely linked to OCD traits which are common in both disorders and an inherent part of their phenotypes (Bejerot *et al.*, 2001, Cassin and Von Ranson, 2005, Russell *et al.*, 2005, Wentz *et al.*, 1999).

Taking all the above information into account, there is some evidence that favours the argument that ED, particularly AN, and ASD may share part of the cognitive endophenotype, namely *weak central coherence*. Weak central coherence in turn would underpin obsessive-compulsive traits, such as perfectionism and a preoccupation with detail (Southgate *et al.*, 2005a), characteristics that maintain AN

(Schmidt and Treasure, 2006). It is likely that this trait would be also relevant for BN based on the obsessive-compulsive phenotype.

More speculatively, the idea that weak coherence underlies the common denominator of OCD traits in AN and ASD opens an interesting pathway to examine the suitability of the shared endophenotype proposal that argues for grouping disorders such as AN and ASD under the umbrella of OCD (Hollander *et al.*, 2007). Some evidence to date supports the proposal. For example, it has been claimed that the high prevalence of OCD in relatives of ASD individuals may be a manifestation of genetic liability vulnerability (Bailey *et al.*, 1998), and that children with autism that are characterised with a narrow range of interest in more likely to have a father with OCD (Hollander *et al.*, 2007).

These ideas will be discussed in the following chapters. The evidence to date that would support the examination of weak central coherence concept in ED is summarised and discussed extensively in Chapter 2.

## 2 CENTRAL COHERENCE IN EATING DISORDERS: A SYSTEMATIC REVIEW<sup>3</sup>

### 2.1 Introduction

This chapter reviews the available evidence from neuropsychological studies on information processing in ED, and more specifically, information processing related to global and detail-focused cognitive styles. The purpose of this review was to systematically appraise the literature that might support or refute the hypothesis that people with eating disorders have *weak central coherence*.

Although from a clinical point of view there is sufficient justification to encourage researchers to explore the weak central coherence hypothesis in ED – e.g. autistic-type traits such as difficulties in social and emotional processing, perfectionist traits, all-or-nothing thinking, extreme focus on calorie counting, body distortion (e.g. Anderluh *et al.*, 2003, Gillberg *et al.*, 1996, Gillberg *et al.*, 1995, Kemps *et al.*, 2007, Zucker *et al.*, 2007) – less is known about the underlying cognitive processes that might explain these behaviours. Therefore, the aim of this review was to collate and summarise a variety of controlled neuropsychological studies looking at aspects of weak central coherence across the ED population and, in this way, to provide the base to the development of the preset thesis.

### 2.2 Background

Recent findings from the study of the neuropsychology of ED have illuminated one potential area that merits interest and future exploration pertaining to the cognitive characteristics of people who suffer from an ED, and particularly AN, that of *weak central coherence*. In a seminal longitudinal study of a community sample of 51 participants with teenage onset of AN evaluated with the Wechsler Adult Intelligence Scale (WAIS; Wechsler, 1981), Gillberg and collaborators (1996) found that the AN group performed worse in the Object Assembly and at a normal to superior level in the Block Design sub-scales yet general performance in the whole

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<sup>3</sup> A version of this systematic review has been accepted for publication in Psychological Medicine as a manuscript entitled ‘Central Coherence in Eating Disorders: A Systematic Review’ (Lopez *et al.*, 2008, in press)

battery of tests did not differ much between both the AN and HC groups. The authors concluded that these results may support the hypothesis that people with AN would have superior ‘concrete thinking’ and deficient ‘abstract thinking’, as proposed by Hilde Bruch based on her clinical observations as early as 1962 (cited in Gillberg *et al.* 1996). Thus, people with AN would tend to approach the world relying more on details rather than wholes. This type of cognitive processing would fit the weak coherence hypothesis in AN. Moreover, as described in Chapter 1, the same study showed that a subgroup of the AN participants (20%) with associated ASD obtained lower scores in the Picture Arrangement sub-scale than the healthy control group. This subgroup of the AN participants exhibited an overall cognitive profile similar to that seen in people with ASD (Ehlers *et al.*, 1997). Cognitive and clinical characteristics (e.g. empathy disorder) seen in some of the people with AN in this study endorse the hypothesis of a possible link between ASD and AN (Gillberg, 1983).

Tokley and Kemps (2007) further explored the hypothesis of impaired abstract thinking in a later study in AN. They found that women with AN obtained lower scores on the Object Assembly task and showed superior performance on the Group Embedded Figure Test (GEFT), a measure of detail-focused processing, relative to a healthy control group. More importantly, they found that the extreme attention to detail manifested in the excellent performance in the GEFT partly explained the deficits found in the Object Assembly task and concluded that the impaired abstract thinking was related to a bias towards detail processing.

More recently, Gillberg and collaborators (2007) replicated their original findings with regards the performance of a sample of subjects with teenage onset of AN on the Object Assembly sub-scale of WAIS in a 6-year follow-up assessment. They argued that this cognitive pattern may indicate that people with AN have weak central coherence. Finally, Southgate *et al.* (2007) found that women with AN had an efficient performance using the Matching Familiar Figures (MFFT) with a superior combination of speed and fewer errors in comparison with a healthy control group. The authors of this study also claimed that the weak central coherence hypothesis might provide a plausible explanation.

The studies mentioned above provide preliminary evidence in favour of the weak central coherence hypothesis in ED, particularly in AN. *Weak central coherence* is thought to explain the cognitive abnormalities present in individuals

with ASD and, based on the aforementioned findings, may also explain the commonality between some individuals with AN and those with ASD (Gillberg *et al.*, 1996, Wentz *et al.*, 1999). Thus the efficient processing of details at the expense of poorer and encumbered global processing seems to be a cognitive characteristic that merits further examination.

### **2.3 Aims and hypothesis**

The purpose of this review was to systematically summarise the evidence to date that would support the hypothesis of weak central coherence in the ED spectrum of disorders. The hypothesis of this study was that people with ED would show superior performance in tasks in which a detail processing style was beneficial and greater difficulties performing in those tasks where a global processing strategy was required.

### **2.4 Methods**

This review follows the Quorum statement for meta-analyses (Moher *et al.*, 1999).

#### **2.4.1 Searching**

The following electronic databases were used to identify relevant papers for inclusion in the review in a two-step search approach: Medline; Embase; Psycinfo; and ISI Web of Science. Searches were conducted in November 2006 and subsequently updated in September 2007.

Two of the studies presented in this thesis (Chapter 4 and 5) were ready by the time of the updated search; however, they were not included in this review in order to reduce researcher bias in the interpretation of the data summarised here.

The two-step searching procedure is described below:

Search one: A literature search was conducted using the term “CENTRAL COHERENCE” to generate all the neuropsychological tests that have been used to

explore this concept in any psychiatric disorder. Afterwards the search was narrowed down to articles in which these tasks were undertaken in people with ED.

Search two: Electronic databases were searched for articles including words related to cognitive assessment in ED. The search included combinations of keywords regarding diagnostic categories (ANOREXIA NERVOSA, BULIMIA NERVOSA, EATING DISORDERS, BINGE EATING DISORDER, BULIMIC DISORDERS), and keywords related to cognitive functioning in ED in general (COGNITION, INFORMATION PROCESSING, NEUROPSYCHOLOGY, COGNITIVE FUNCTIONING, COGNITIVE STYLES, LOCAL/GLOBAL PROCESSING, FIELD DEPENDENCY / INDEPENDENCE, WHOLISTIC / ANALYTIC STYLE, ABSTRACT THINKING) to ensure that papers not explicitly advertising the use of the mentioned tasks would be included.

Following the initial identification of relevant published articles all citations were then obtained. Key investigators currently conducting research in the field were contacted with requests for any unpublished material. Manual searching of relevant references in each citation was also carried out.

Thirty-five tests were generated from the search on the central coherence concept and these came mainly from ASD literature. Two published articles utilised the concept in ED (Gillberg *et al.*, 2007, Southgate *et al.*, 2007).

After search two, only the following relevant tests were found to have been used in ED: the BLOCK DESIGN and OBJECT ASSEMBLY subscales of the Wechsler Intelligence Scales, GROUP/EMBEDDED FIGURES TEST, REY-OSTERRIETH COMPLEX FIGURE, MATCHING FAMILIAR FIGURES, and CALIFORNIA VERBAL LEARNING TEST.

#### 2.4.2 Selection

The search was conducted by one researcher (CL) and was then duplicated by volunteer research assistants who gathered the data on the basis of the following inclusion criteria:

a. Population – participants suffering or recovered from an ED *and* a healthy control group (HC).



b. Instruments – studies specifying the use of one of the tasks measuring aspects of local or global processing as mentioned before.

c. Study designs – cross sectional studies. Repeated measures from the single identified longitudinal study were included separately.

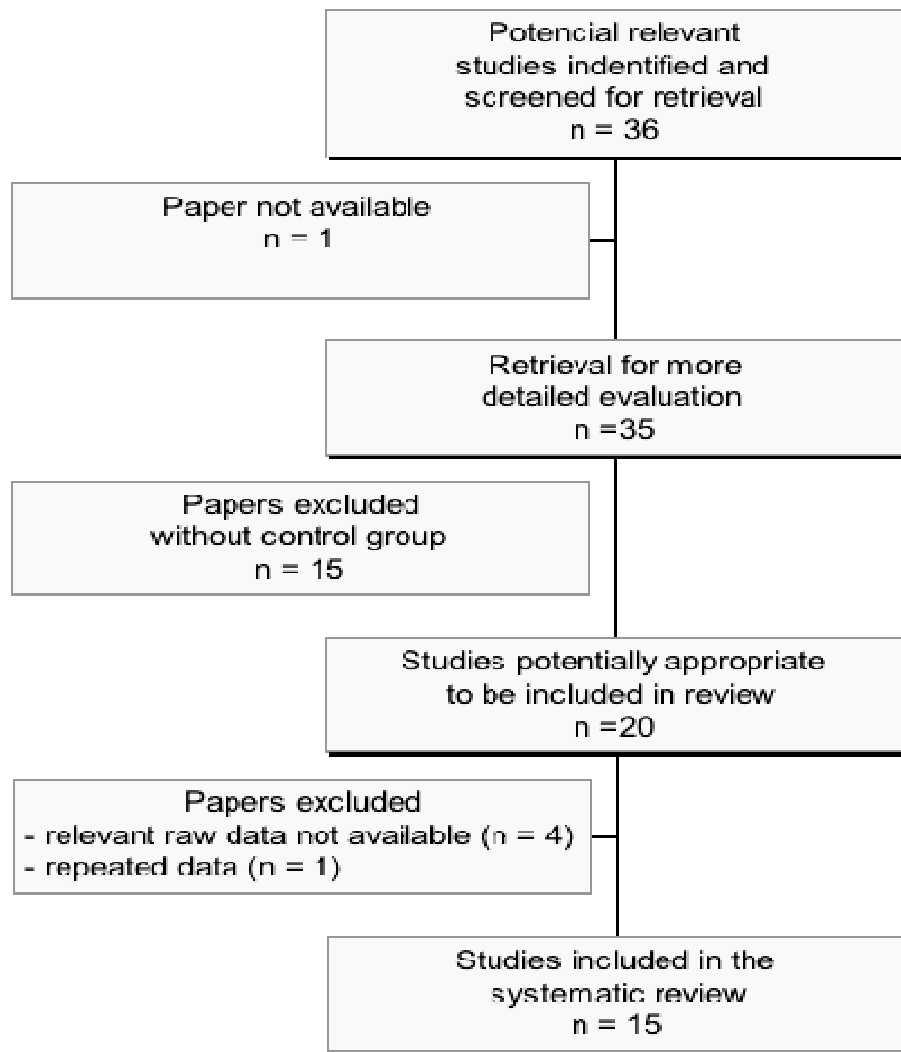
The outcome variable was functioning on the information processing aspect of the tasks.

#### 2.4.3 Data abstraction

Thirty-six relevant abstracts of studies using the aforementioned tests were found and the full papers were retrieved. It was not possible to obtain one paper as we could not contact the author (Talarczyk and Rajewski, 2001). Fifteen of the remaining studies were excluded as they did not include a HC group (Bayless *et al.*, 2002, Bowers, 1994, Dura and Bornstein, 1989, Gordon *et al.*, 1984, Hamsher *et al.*, 1981, Kaye *et al.*, 1995, Key *et al.*, 2006, Kitabayashi *et al.*, 2004, McDowell *et al.*, 2003, Nakasuji, 1999, Ranseen and Humphries, 1992, Small *et al.*, 1983, Small *et al.*, 1982, Sours, 1969, Touyz *et al.*, 1986). Some papers did not report adequate raw data required for this review. The corresponding author was contacted in such cases, if the study was published after 1996, and asked to provide the raw data. Four studies were eliminated because the relevant outcomes were unavailable (Bradley *et al.*, 1997, Fox, 1981, Horne *et al.*, 1991, Steinglass *et al.*, 2006). Finally, one study reported previously published data (Murphy *et al.*, 2004), therefore only the first published study was utilised (Murphy *et al.*, 2002). Data from one published study included repeated measures in a longitudinal study (Gillberg *et al.*, 2007). These data were included in the review table but were excluded (because of lack of independence) from the meta-analysis.

In summary, this systematic review included 15 studies.

**Figure 2.1** displays the flowchart showing the selection process and the results following the Quorum statement procedures.



**Figure 2.1** Flowchart selection of the studies for systematic review

#### 2.4.4 Description of the tasks

Most of the studies that provided the data required for the systematic review were not designed for the purpose of exploring global and detail-focused processing of information but other aspects of cognitive functioning (e.g. intellectual coefficient, cognitive impulsivity, etc). A detailed explanation of how these data were interpreted is therefore provided below in the description of tasks.

Moreover, the available studies in the field of ED have focused on visual-spatial abilities and have not included other cognitive domains (e.g. auditory/verbal) where weak central coherence might manifest.

According to the review of the central coherence account in ASD by Happé and Frith (2006) tasks that would benefit from a detail-focused approach are:

##### **2.4.4.1 *The Block Design Task (BD)***

This task has usually been utilised in ED populations as part of the Wechsler Intelligence Scales (Wechsler, 1974, 1981, 1991, 1997) and will be fully described in Chapter 3.

It has been argued that faster performance on this task may indicate a better detailed visual processing (weak central coherence) as it relates to the ability to automatically segment the designs into their component parts (Shah and Frith, 1993). This hypothesis has been proven using a modified version of the task in which performances in two conditions of the design presentation are compared: unsegmented (whole designs) and segmented designs (designs are broken into their 4 or 9 constituents parts). The weak central coherence hypothesis predicts that those with enhanced detail-focused processing style would benefit less from the segmentation of the designs in comparison with those with a predominant global processing style, as a result of their natural ability to segment the whole into its details (Happé *et al.*, 2001, Shah and Frith, 1993). However, this version has not been used in the ED population. Therefore, the original version of the block design test was utilised in this review and the assumptions generated by the ASD literature were accepted as true.

#### **2.4.4.2 *Embedded Figures Test (EFT)/Group Embedded Figures Test (GEFT)***

Witkin *et al.* (1971) developed the original version of the Embedded Figures Test. The same author then developed a version that is suitable for group administration, the Group Embedded Figures Test (Witkin *et al.*, 2002). The results of these tests have been traditionally interpreted as a measure of field dependence/independence (Spreen and Strauss, 1998). Field independent individuals are those who can efficiently process information thanks to their ability to narrow their focus and to resist the predominance of background information (Witkin *et al.*, 1971). They are, therefore, good at identifying details over the gestalt. Although there is a conceptual difference between field independency and weak central coherence (for a revision see Happé and Frith, 2006) both accounts predict a successful performance on the EFT task. Scores on these tasks are expressed in seconds and represent the time taken to locate the hidden shapes. A shorter time has been described as a result of a strong local processing or a bias toward detail (Baron-Cohen and Hammer, 1997, Jolliffe and Baron-Cohen, 1997). Also, a measure of accuracy (number of time-out errors) has sometimes been used. More details about this task can be found in Chapter 3.

#### **2.4.4.3 *The Matching Familiar Figures Test (MFFT)***

This visual perceptual test was designed to measure cognitive impulsivity (Kagan, 1966, Kagan *et al.*, 1964). It consists of 12 items, for each of which the participant is asked to identify the exact replica of a familiar object (e.g. a lion) amongst 8 very similar alternatives. The time latency to identify the “matching” figure and the number of errors, are recorded. Four categories of the predominant thinking style (‘reflective’ versus ‘impulsive’ and ‘efficient’ versus ‘inefficient’) have been traditionally used (Glow *et al.*, 1981). Shorter time latencies with more errors have usually been associated with a more ‘impulsive’ cognitive style whereas longer latencies with fewer errors have been associated with a ‘reflective’ processing style. Also, a fast performance with few errors (accurate) is categorised as ‘efficient’ while a slow and inaccurate performance comes under the ‘inefficient’ category. A dimensional approach has also been introduced in which a combination of time latency and errors is entered into equations to provide dimensional scores for the above categories i.e. ‘reflection-impulsivity’ and ‘efficiency-inefficiency’ (Salkind

and Wright, 1977). Individuals with a more detail focused processing are thought to have both reduced time and errors (better ‘efficiency’).

The following tasks were conceptualised as measures of efficient global processing:

#### ***2.4.4.4 The Object Assembly Task (OA)***

Object assembly is also one of the performance tasks of the Wechsler Intelligence Scale (Wechsler, 1974, 1981, 1997). This task involves solving small jigsaw type puzzles depicting familiar objects such as a butterfly or a horse. Time taken to complete the puzzles is a measure of performance together with the total number of puzzles completed within the designated time. A shorter time suggests a better ability to create an integrated global representation from its individual parts (Tokley and Kemps, 2007), therefore, successful performance would mirror efficient use of global processing strategies.

#### ***2.4.4.5 The Rey-Osterrieth Complex Figure Test (RCFT)***

This well known drawing test assesses a variety of cognitive processes including: visual perceptual organization, non-verbal memory, planning, problem solving and motor function (Osterrieth, 1944). A full description of this task is provided in Chapter 3, as this is one of the tasks used in the experimental studies of this thesis. Participants are asked to copy the diagram of a complex figure. After an interval of time (that varies from 3 to 60 min), during which the original diagram of the figure has been removed without prior warning, they are asked to recall and draw the figure. *Accuracy* in the copy and recall drawing has usually been the main outcome for this task and the degree of recall accuracy has been understood as a result of the efficiency of visual memory (Lezak *et al.*, 2004, Osterrieth, 1944, Spreen and Strauss, 1998). However, experimental studies have shown that organisation in the process of drawing (whether the individual focuses on details or global elements of the figure when copying it) affects the percentage of recall (Strauss *et al.*, 2006). Several process measures for organizational strategy have been developed. In the field of ED the only method to be employed has been developed by

Savage and collaborators (1999) and has been widely used in the study of obsessive-compulsive disorders and other anxiety related disorders (Bohne *et al.*, 2005, Deckersbach *et al.*, 2000, Savage *et al.*, 2001, Savage *et al.*, 2000). Savage *et al.* (1999) have demonstrated that the organisational strategies displayed by the participant during the copy of the figure mediate the accuracy in the recall trial. Thus, a global drawing style favours recall and a detail focused style influences it negatively. Therefore, this mediation hypothesis provides the background for the possibility of interpreting the poor results in recall accuracy as an index of information processing. For more details about this task please see Chapter 3.

#### 2.4.5 Quantitative data synthesis

This review used meta-analysis as the main statistical method. A meta-analysis is a set of statistical procedures that allows for the integration of findings from several independent studies that address the same hypothesis, thereby increasing the statistical power of studies with small sample sizes and combining the effect sizes in a standardised manner (Cooper and Hedges, 1994, Streiner, 1991).

Outcomes clustered by tasks were summarised by a meta-analysis if the number of comparisons between ED and HC groups available were  $> 5$ . Thus, it was possible to carry out a meta-analysis for most of the tasks, i.e., the Block Design Task, the Embedded Figures Test, the Rey-Osterrieth Figure Test (accuracy) and the Object Assembly Task. Meta-analyses were carried out in Stata 9.1.

First, standardised *Cohen's d* effect sizes - the difference between ED and HC divided by the pooled standard deviation - were calculated for each comparison using an effect size calculator program (Wilson, 2001). *Cohen's d* is understood as *negligible* ( $\geq 0$  and  $< 0.15$ ), *small* ( $\geq 0.15$  and  $< 0.40$ ), *medium* ( $\geq 0.40$  and  $< 0.75$ ), *large* ( $\geq 0.75$  and  $< 1.10$ ), *very large* ( $\geq 1.10$  and  $< 1.45$ ) and *huge* ( $> 1.45$ ).

The standardised effect sizes were subsequently analyzed using the user-contributed command *metan* (Bradburn *et al.*, 1998). The standard error of each study's standardised effect size was calculated using the method by Cooper and Hedges (1994) and pooled using a random-effects model. Random effects models allow for the exploration of variation of effect sizes between studies (Everitt, 2003).

The homogeneity between the studies was evaluated using the Cochran's Q test. Due to the small sample sizes of the studies included by task an additional measure of heterogeneity or inconsistency  $I^2$  ( $(Q-df)/Q$ ) was calculated (Higgins *et al.*, 2003).  $I^2$  ranges between 0% (no inconsistency) and 100% with values of 25%, 50% and 75% were indicative of low, moderate and high heterogeneity, respectively.

The presence of publication bias was assessed informally by visual inspections of funnel plots which were corroborated formally by their corresponding statistical analogue, Begg's adjusted rank test (Begg and Mazumdar, 1994), and additionally by Egger's test (Egger *et al.*, 1997) as executed using the command *metabias* (Steichen, 1998). The Trim-and-fill method for adjusting for publication bias was employed when necessary (Duval and Tweedie, 2000).

Forest plots were used to display meta-analyses results. A forest plot "provides a simple visual representation of the amount of variation between the results of the studies, as well as an estimate of the overall result of all the studies together with all the independent data available for each measure" (Lewis and Clarke, 2001, p. 1479). Each line in the forest plot represents an individual study/comparison. The position of the square in relation to the vertical axe, represents the point estimate of the results of a particular study; specifically it shows how the effect size of the study varies from zero. The size of the square shows the weighed individual contribution of the study to the meta-analysis and it is proportional to the sample size of the study. The horizontal line through the square represents the 95% Confidence Interval (CI) of the effect size. The overall estimate from the meta-analysis and its CI are displayed at the bottom of the plot represented as a diamond.

The effect size obtained in studies including repeated measures are reported in text only in order to avoid the overrepresentation of certain samples, corresponding to longitudinal studies, in the overall effect size obtained through the meta-analyses.

The Matching Familiar Figures Test was the only task that could not be summarised in a meta-analysis due to the small number of studies that utilised this task and found to be suitable for this review and for which only *Cohen's d* individual effect sizes (*d*) were calculated. The same procedure was employed for the organisation strategies of the Rey-Osterrieth Complex Figure as used in only one study.

## **2.5 Results**

### **2.5.1 Study characteristics**

All the studies presented here used a controlled cross-sectional design. Table 2.1 presents a summary of the main characteristics of the studies included in the review. Most of the studies (n=13) compared people with anorexia nervosa (AN) with a HC group. Only 6 studies included people with bulimia nervosa (BN). One study included a group of weight-recovered women following a period of acute AN (WRAN). Two studies included mixed AN groups i.e. patients at various stages of illness (combination of patients with acute illness, partial recovery and/or full recovery).



**Table 2.1 Characteristics of the studies included in this review**

Study	Sample		Age	BMI	IQ	Meds.	Co-morbidity	Groups	BD	EFT	MFF		ROFT		OA
	Group	n									Time	Errors	Time	Acc Copy	
Basseches et al. (1984)	AN	16	19.8 (2.0)	>25% normal weight	115.0 (11.14)	n.r.		AN v HC		-1.02 *					
	HC	16	19.8 (2.5)		117.0 (6.30)	n.r.									
McLaughlin et al. (1985)	AN	25	23	16,64	n.r.	n.r.		AN v HC		0.84 *					
	BN	25	24.8	21,26	n.r.	n.r.		BN v HC		1.05 *					
	HC	25	23.6	20,74	n.r.	n.r.									
Toner et al. (1987)	Mixed ANR	23	27.4 (5.3)	84% of average	n.r.	n.r.		ANR v HC			0.02	0.02			
	Mixed ANBN	21	28.6 (4.0)	82.8% of average	n.r.	n.r.		ANBN v HC			0.81*	0.07			
	HC	24	27.2 (5.3)	89% of average	n.r.										
Pendleton-Jones et al. (1991)	AN	30	24.4 (5.3)	59.4 (6.6) % ideal	103.9 (11.2)	No	47% Dep; 3% Bipolar; 7% other Dep; 7% SA	AN v HC	-0.74 *	0.72 *					-0.40 *
	BN	38	24.1 (4.0)	94.0 (7.3) % ideal	109.0 (10.9)	No	26% Dep; 3% Bipolar; 39% other Dep; 5 SA	BN v HC	-0.67	0.47					-0.12
	WRAN	20	26.0 (6.2)	87.8 (11.2) % ideal	111.4 (15.9)	No	50% Dep; 35% other mood disorders; 5% SA	WRAN v HC	-0.39	0.80*					-0.30
	HC	39	24.9 (4.4)	98.2 (7.5) % ideal	113.5 (11.8)	No									

Legends: AN= Anorexia Nervosa; HC= Health Control; WRAN= Weight recovered AN; ANBN= Bulimic Anorexic patients; IQ= intellectual ability; Meds.= use of medicines; Groups= group comparison; Dep= Depression; SA= Substance Abuse; n.r.= Not reported; \*= Significant difference between groups ( $p<0.05$ )

**Table 2.1. Continuation...**

Study	Sample		Age	BMI	IQ	Meds.	Co-morbidity	Groups	BD	EFT	MFF		RCFT		OA
	Group	n									Time	Errors	Time	Acc Copy	
Szmukler et al. (1992)	AN	21	matched	14.7 (1.9)	matched	No		AN v HC	-0.74 *						
	HC	18		n.r.		No									
Thompson (1993)	AN	10	25.8	>15% normal weight	115.8		40% Dep; ↑OCD	AN v HC	0.50			-1.51 *			-1.17 *
	HC	10	23.2	n.r.	119.7										
Kingston et al. (1996)	AN	46	22.1 (6.7)	14.7 (1.7)	108.9 (5.7)	33%	↑Anx; ↑Dep	AN v HC	-0.37 *			-0.25			-0.30
	HC	41	22.0 (5.8)	22.1 (1.9)	109.0 (6.3)	No									
Gillberg et al. (1996)	Mixed AN	51	21	21.2 (3.5)	102.9		10 ASD	Mixed AN v HC	-0.30						-0.65
	HC	51	20.8	21.2 (2.3)	106.5										
Mathias & Kent (1998)	AN	34	22.7 (7.4)	15.3 (1.7)	96.1 (8.8)*	33%	↑Anx; ↑Dep	AN v HC	-0.43			-0.52			-0.67 *
	HC	31	20.8 (2.4)	22.8 (2.4)	101.1 (6.9)*	No									
Murphy et al. (2002;2004)	AN	16	22.3 (4.4)	14.8 (1.2)	119.3 (9.8)	13%	↑OCD	AN v HC				-0.18			-0.45
	BN	16	22.0 (4.5)	20.1 (2.3)	122.7 (4.3)	25%		BN v HC				-0.18			0.61 *
	HC	16	25.3 (2.6)	22.0 (2.6)	117.1 (5.6)	No									

Legends: AN= Anorexia Nervosa; HC= Health Control; WRAN= Weight recovered AN; ANBN= Bulimic Anorexic patients; IQ= intellectual ability; Meds.= use of medicines; Groups= group comparison; ↑ = higher than HC in the trait reported; OCD= Obsessive-Compulsive Disorder; Anx= Anxiety Disorder; Dep= Depression; ASD= Autistic Spectrum Disorders; n.r.= Not reported; \*= Significant difference between groups ( $p<0.05$ )

**Table 2.1. Continuation...**

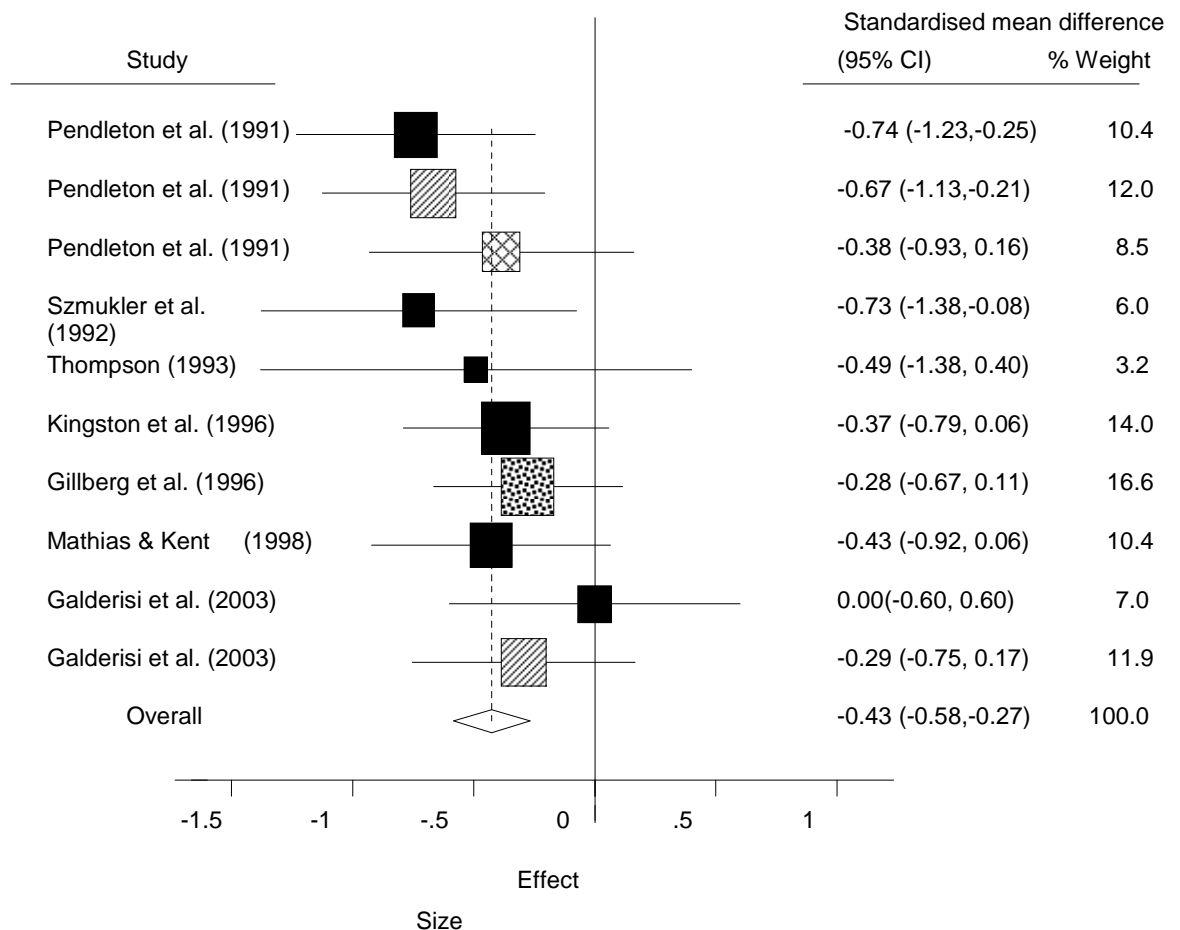
Study	Sample		Age	BMI	IQ	Meds.	Co-morbidity	Groups	BD	EFT	MFF		RCFT		OA
	Group	n									Time	Errors	Time	Acc copy	
Galderisi (2003)	AN	14	23.7 (4.5) **	15.3 (2,23)	100 (10.8)**	No		AN v HC	0						0.31
Galderisi (2003)	BN	31	23.7 (4.54)	21.5 (2.30)	100 (10.8)	No	4 Dep, 3 pd disorders	BN v HC	-0.29						-0.45
	HC	45	24.2 (4.8)	Nr	101.1 (13.6)	No									
Sherman et al. (2006)	AN	18	25.6 (5.8)	16.7 (1.1)	n.r.	61%	6 Dep; 3 Dysth; 5 GAD	AN v HC				-0.64 *	-0.87 *	-1.42 *	
	HC	19	25.7 (5.3)	22.2 (1.8)	n.r.	No									
Gillberg et al. (2007)	Mixed AN	47	24.5	22.2 (4.1)	105.2 *			Mixed AN v HC	0.3						-0.46 *
	HC	51	24.2	22.2 (3.4)	109.4										
Southgate et al. (in press)	AN	20	26.8 (8.5)	16.3 (2.6)	116.8 (4.8)	No	↑OCD; ↑Anx; ↑Dep	AN v HC			-0.38	-0.3			
	BN	14	25.7 (4.9)	21.1 (6.7)	114.4 (7.3)	No	↑Anx; ↑Dep	BN v HC			-0.34	-0.01			
	HC	26	27.3 (11.5)	22.0 (3.4)	114.8 (5.8)	No									
Tockley & Kemps (2007)	AN	24	21.9 (5.3)	16.8(1,5)	matched	n.r.	↑OCD; ↑Anx; ↑Dep	AN v HC		-0.75 *					-0.31 *
	HC	24	22.0 (5.0)	22.7 (4.3)											

Legends: AN= Anorexia Nervosa; HC= Health Control; WRAN= Weight recovered AN; ANBN= Bulimic Anorexic patients; IQ= intellectual ability; Meds.= use of medicines; ↑ = higher than HC in the trait reported; n.r.= Not reported; Groups= group comparison; \* =  $p < 0.05$ ; \*\* The authors reported Age and IQ grouping AN and BN

## 2.5.2 Summary by task

### 2.5.2.1 Block Design Test (BD)

BD was used in 7 studies (see Table 2.1.). Generally, BD was used as part of the full or partial standard measure of intelligence quotient (WAIS, WISC). There were no studies in ED using the new development of the task created to assess central coherence (Shah and Frith, 1993). A meta-analysis was carried out including all the studies (see Figure 2.2). It revealed a moderate pooled standardized effect size ( $d = 0.43$ ) indicating that people with ED are, generally speaking, slower than HC groups in constructing replicas of the designs from blocks ( $z = 5.24, p < .001$ ).



**Figure 2.2 Forest plot of Block Design meta-analysis**

(AN ■ ;BN ▨;mixed AN ▩; WRAN: ▤ )

The meta-analysis showed no evidence of heterogeneity across studies ( $X^2_{(9)} = 6.38, p = 0.70$ ), and also, the effect sizes were found to be consistent ( $I^2=0.0\%$ ). Finally, Begg's and Egger's tests and funnel plots showed no evidence of publication bias (all  $p>.50$ ). When taking into account only AN groups, a meta-analysis revealed similar results, that is that in general, people with acute AN perform more poorly than HC on this task ( $d = 0.42, 95\% \text{ CI} = 0.61 - 0.22$ ).

Although in general people with ED perform poorer than HC, only two of the studies had reported statistically significant differences (Pendleton Jones *et al.*, 1991, Szmukler *et al.*, 1992). A thorough review of the studies revealed no explanations as to why their results were atypical. It is possible that the larger effect size found in Pendleton Jones *et al.*'s study (1991) may have been confounded by the lower intellectual ability levels in ED groups in comparison to the HC group, as it is known that the BD task is one of the best predictors from the Wechsler Adult Intelligence Scale of intellectual ability (Spreeen and Strauss, 1998, Strauss *et al.*, 2006). Participants with BN also showed poor performance on this task (Galderisi *et al.*, 2003, Pendleton Jones *et al.*, 1991).

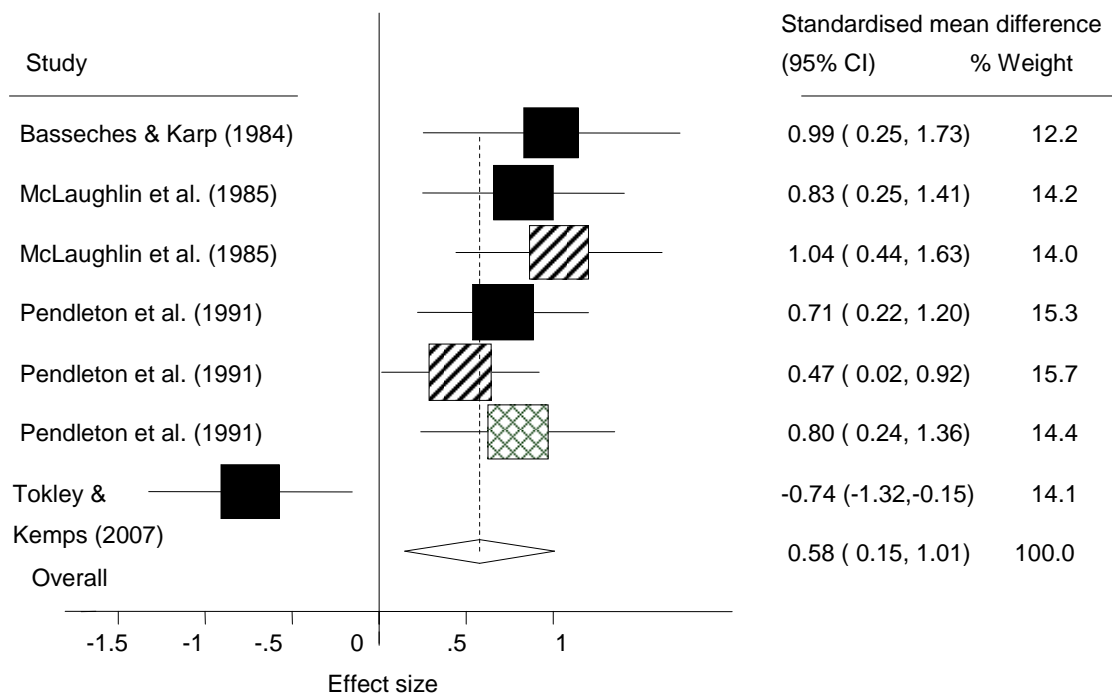
A meta-analysis including repeated measures of a group after refeeding (Szmukler *et al.*, 1992) and a group 10 years after onset (Gillberg *et al.*, 2007), revealed an overall effect size of  $d = 0.41$  (95%  $\text{CI}=-0.55,-0.26$ ). This finding may suggest that although the performance of people with AN on this task seems to improve after weight recovery it may remain somewhat impaired. However, none of these studies found significant differences between the ED and the HC group.

#### **2.5.2.2 Embedded Figures Test (EFT)**

The EFT was used in 4 studies, which yielded a total of 7 comparison studies between ED and HC groups (see Figure 2.3). All the studies included an AN group; two a BN group; one involved recovered people (WRAN). One study (Basseches and Karp, 1984) also administered the test to an obese group. The latter was not included in the meta-analysis as this population was outside the inclusion criteria but the study revealed that obese people performed poorly on the EFT in comparison to AN and HC groups ( $d = -1.3$ ).

The meta analysis revealed a high degree of heterogeneity across the studies ( $X^2_{(6)}= 24.8, p < .001$ ). The index of inconsistency between studies reached 75.8%.

Despite this heterogeneity, the effect size found here was significant ( $z = 2.63, p = .008$ ). Beggs's and Egger's tests revealed a statistical trend for publication bias ( $p = .10$  and  $p = .81$ ), corroborated by a visual inspection of the funnel plot. After the trim-and-fill procedure, the standardised effect size slightly decreased to  $d = .57$ . Begg's funnel plot suggests a lack of studies with large positive effect sizes and/or an overrepresentation of negative effect studies. There is therefore a possibility of underestimating the effect sizes due to a publication bias. Also, it might be possible that the new studies are different to the old ones. This hypothesis will be discussed later.



**Figure 2.3 Forest plot of EFT meta-analysis**

(AN ■ ;BN ▨ ; WRAN: ▩ )

There appears to be a distinction between the studies carried out before 1991 and the most recent identified study. The earlier studies found that people with ED took longer on this task. These studies were examined in more detail in order to find explanations for the contradictory results. There maybe technical and administration differences. All the reported studies, with the exception of that by Tokley and Kemps (2007) which used the GEFT adapted for individual administration, used the original EFT. The procedure for the GEFT is clearly defined; participants can check the “hidden” shape as many times as they need while searching for it in the complex figure. None of the studies using the original version of the task gives a detailed description of the procedure employed and a manual based procedure is assumed but not explicitly stated: the simple shape is shown once and removed while the participants is searching for it in the complex figure. It is possible that the memory component involved in the original manner of administrating the task interferes with the ability to locate the ‘hidden’ shape in people with AN, who may present working memory difficulties (Southgate et al., 2006). Therefore, the modification in the administration involved in the GEFT can better explain the results in ED groups when no working memory is required to perform in the test. Also, in two of the studies where ED groups performed poorer (Basseches and Karp, 1984, Pendleton Jones *et al.*, 1991) their IQ was lower than in HC and this may have confounded the results as there is some evidence that performance on the EFT is related to intellectual ability (Flexer and Roberge, 1980, Riding and Pearson, 1994).

### **2.5.2.3 Matching Familiar Figures Test (MFFT)**

Only two studies using the MFFT fulfilled the criteria for inclusion in this review (Southgate *et al.*, 2007, Toner *et al.*, 1987). Toner and collaborators (1987) found that patients with a bulimic type of AN made more errors than the HC ( $d = 0.81$ ) and the restricting type of AN ( $d = 0.74$ ). They found no differences in terms of response latency. Some of the patients in the AN group were in partial recovery at the time of the study. Those with binge-purging AN were the fastest group ( $d = 0.41$ ) but the least accurate, i.e. made more errors ( $d = 1.23$ ) which is indicative of an impulsive cognitive style. Southgate *et al.* (2007) reported no statistical differences across groups (AN, BN and HC) in number of errors, response

latency and the impulsivity index. However, ED groups were in general faster and more accurate than HC. They also found higher efficiency in the AN group in comparison with people with BN and HC e.g. the AN group was faster and more accurate in completing the task ( $d = 0.89$ ).

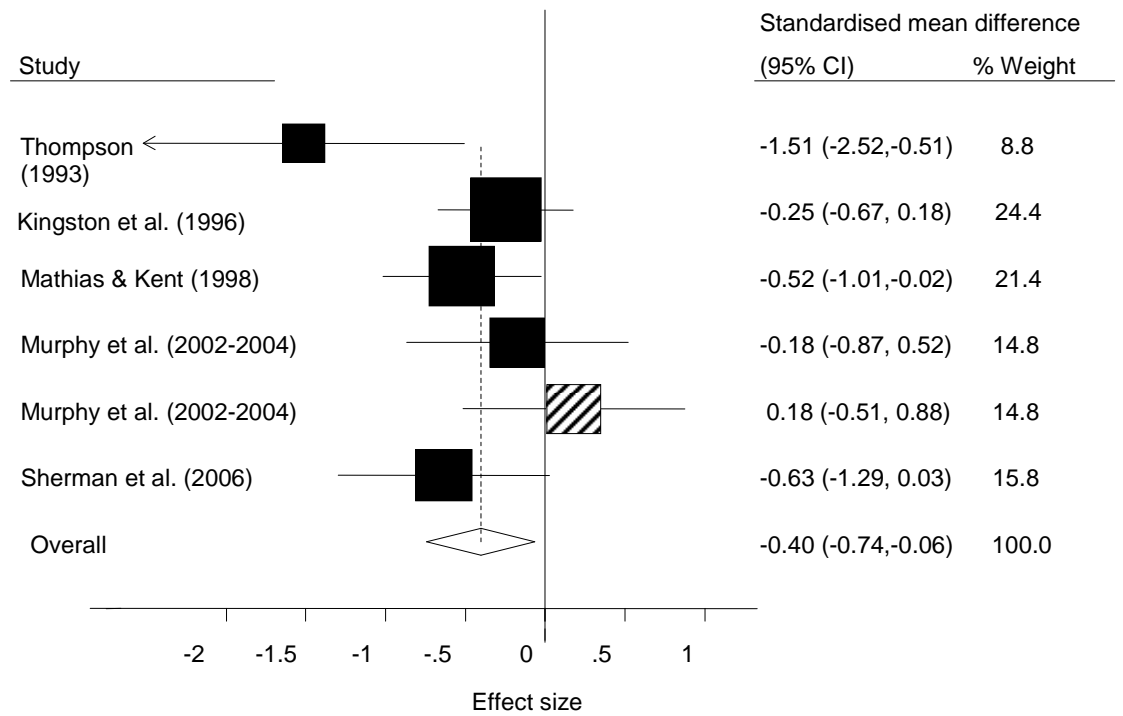
Differences in terms of stages of illness as well as the diagnostic sub-grouping may explain some differences across studies in the number of errors recorded. More studies using the impulsivity and efficiency indices are needed.

#### **2.5.2.4 Rey - Osterrieth Figure Test (RCFT)**

**COPY ACCURACY:** Five studies utilized the RCFT copy trial with an AN sample (Kingston *et al.*, 1996, Mathias and Kent, 1998, Murphy *et al.*, 2002, Sherman *et al.*, 2006, Thompson, 1993) and were integrated in the meta-analysis (see Figure 2.4). One of the studies also included a BN group (Murphy *et al.*, 2002). The meta-analysis revealed a significant moderate effect size ( $d = 0.40$ , 95% CI = -0.74 to -0.06). Overall, people with ED were less accurate than HC in copying the diagram. This meta-analysis showed moderate heterogeneity ( $X^2_{(5)} = 8.96$ ,  $p < .111$ ,  $I^2 = 44.2\%$ ), mainly due to one of the studies, the results of which constitute an outlier (Thompson, 1993). Inspection of this study, in which the effect size was larger than in other studies suggesting that the AN group obtained much lower scores in copy accuracy, revealed a failure to match groups that could account for these differences (Mathias and Kent, 1998). This study did consider the effect of confounding variables such as depression.

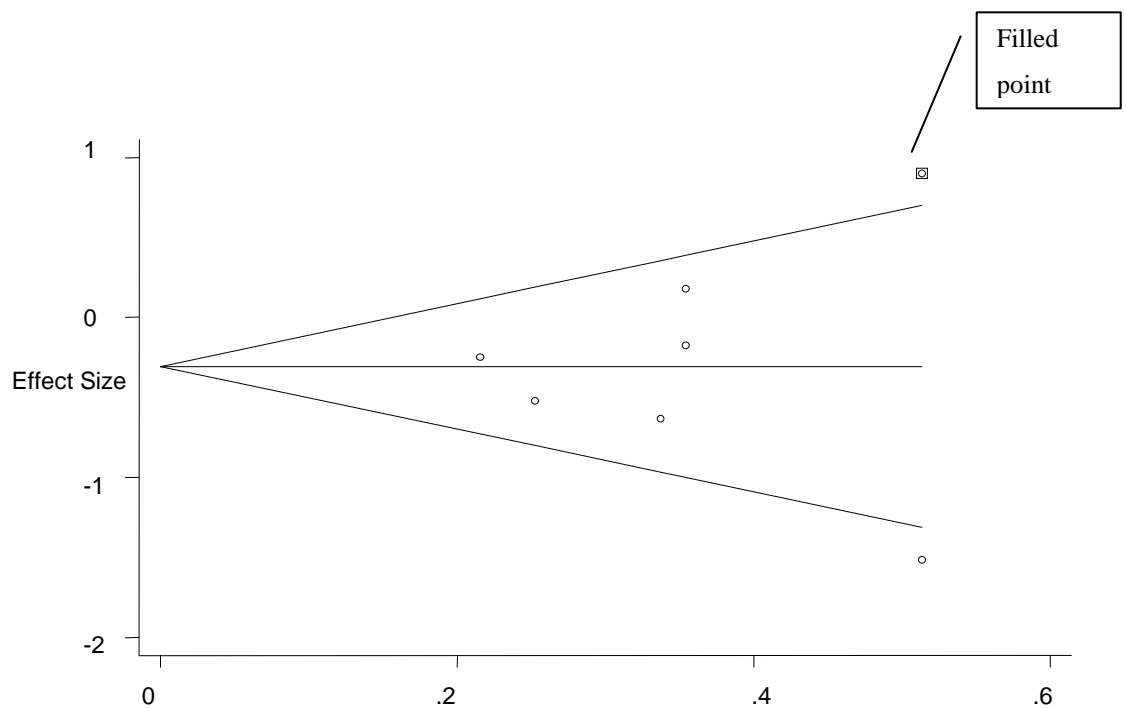
Even though no publication bias was found using statistical methods (Egger's and Begg's tests  $p > .41$ ), trim-and-fill methods for adjusting for publication bias estimated that one study was missed by the meta-analysis (see Figure 2.5) thereby compensating for the extremely large effect of Thompson's study (1993). With this correction, the overall effect size found in the meta-analysis decreased to  $d = 0.30$  (95% CI = -.69, 0.10).





**Figure 2.4 Forest plot for accuracy in copy RCFT meta-analysis**

(AN ■;BN ▨)



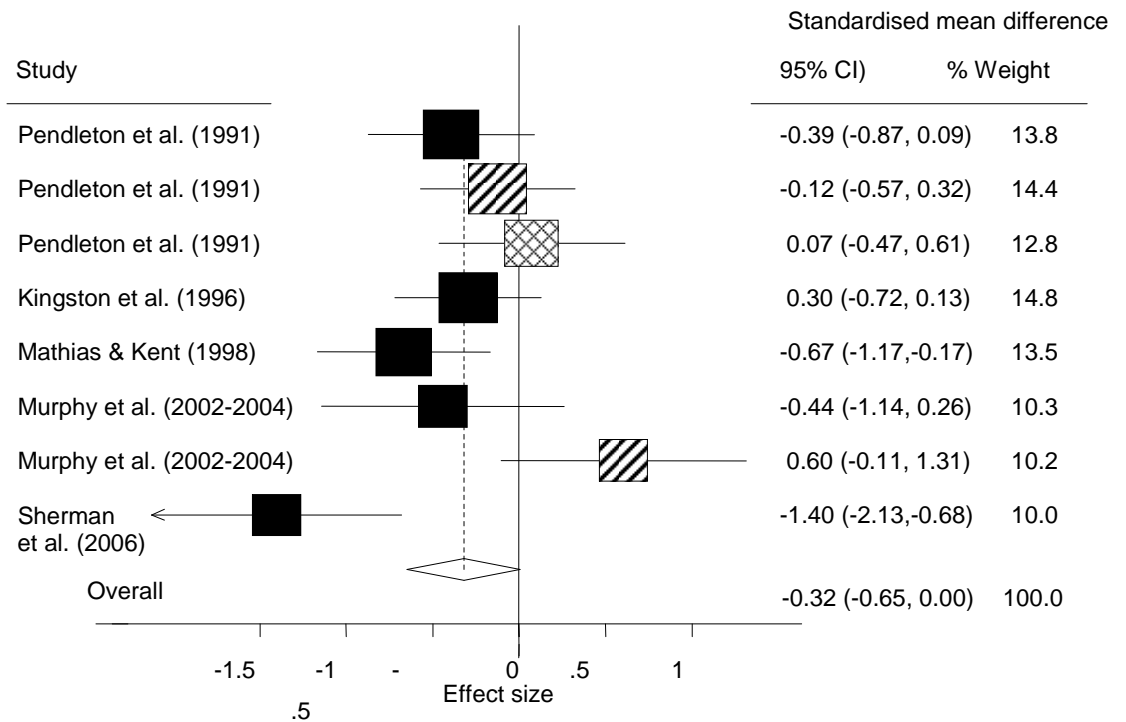
**Figure 2.5 Filled funnel plot with pseudo 95% confidence limits for RCFT copy trial after trim-and-fill procedure**

**RECALL ACCURACY:** Five studies used a delayed recall test of RCFT in the AN population, two studies included a BN population, and one evaluated a group of recovered AN (see Figure 2.6). One of the studies included immediate recall (e.g. Sherman *et al.*, 2006) but it was not included in the meta-analysis; only delayed recalls were taken into account to preserve independency of data and to use only those data that would be more comparable with each other. The time intervals between copy and delayed recall varied across the studies. Four studies used 30 minutes (Kingston *et al.*, 1996, Mathias and Kent, 1998, Murphy *et al.*, 2002, Sherman *et al.*, 2006) and one did not report the time interval (Pendleton Jones *et al.*, 1991).

The meta-analysis excluding the repeated measures revealed an overall effect size of  $d = -0.32$  and moderate indices of heterogeneity ( $X^2_{(7)} = 19.9$ ,  $p = .006$ ;  $I^2 = 64.9\%$ ). The moderate heterogeneity could be due to the inclusion of populations with different diagnoses and at different stages of the illness that performed differently on the task. Particularly, the performance of BN groups was inconsistent in the two studies included in the review. The effect size of these studies varied from  $d = -0.12$  to  $d = 0.60$ . Murphy and collaborators (2002) reported a superior performance by the BN group whereas Pendleton *et al.* (1991) obtained opposite results. Intellectual differences (IQ) and age of the participants may confound these results.

Sherman *et al.* (2006) found the largest effect size in comparison with the rest of the studies including AN groups, which also constitutes an outlier. Possible explanations for the very poor performance of the AN group in this study might be the high co-morbidity with anxiety disorders and depression and the fact that over 60% of the sample were on medication. The AN group in this study had lower scores even on the copy trial ( $p = .06$ ,  $d = 0.63$ ). Overall, these results show that people with AN recall significantly less than HC in the RCFT.

No evidence of publication bias was found (Egger's and Begg's tests  $p > .71$ ).



**Figure 2.6 Forest plot for accuracy in recall RCFT meta-analysis**

(AN ■ ;BN ▨; WRAN: ▩ )

**ORGANISATIONAL STRATEGIES:** Only one of the reviewed studies explored the process of the copy of the RCFT (Sherman et al., 2006). This study replicated the observations from studies of obsessive-compulsive populations (Savage et al., 1999) confirming that the organisational approach while copying the RCFT explained the deficit in visual memory in the recall by mediating the effect of grouping (e.g. AN vs. HC). The study found an effect size of  $d=.87$  for AN meaning that the process of drawing in the latter was fragmented, focused on detail and lacking in organisation.

### 2.5.2.5 Object Assembly (OA)

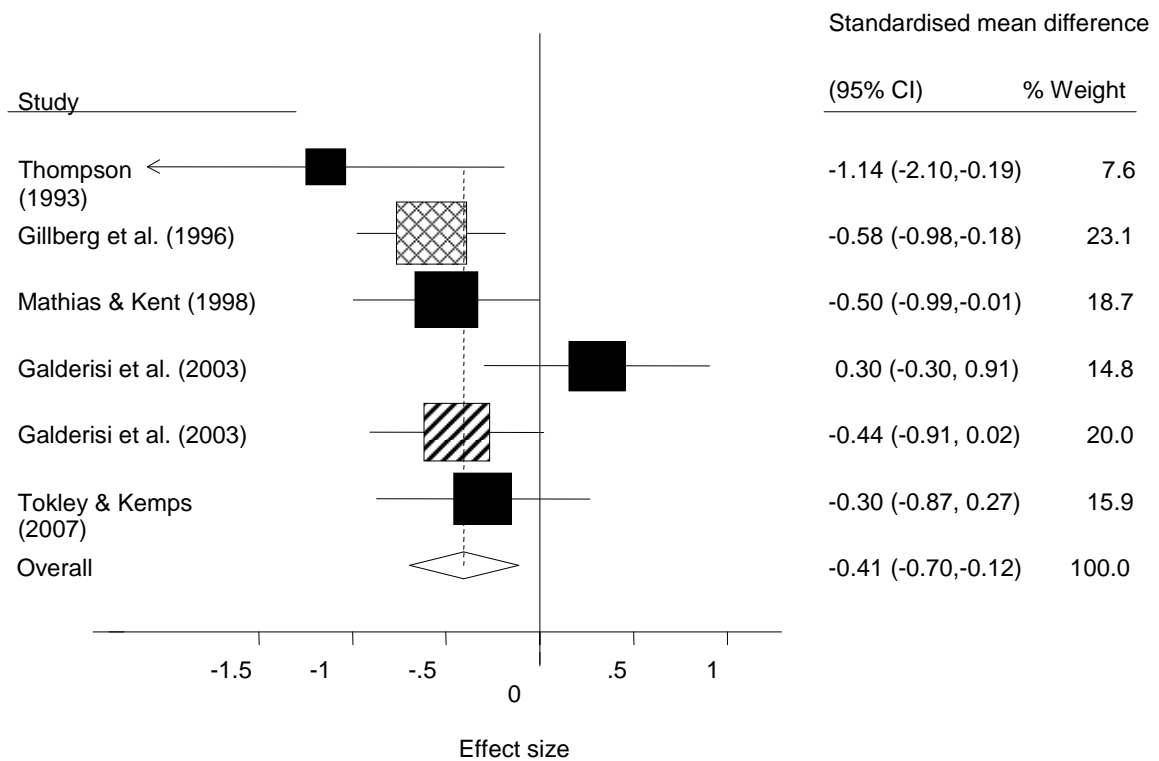
This task was used in six of the studies comparing groups with AN or mixed AN and HC. Only one included a group of women with BN (see Figure 2.7).

The results from the meta-analysis revealed a moderate effect size across the studies ( $d = 0.41$ ,  $z = 2.74$ ,  $p = .006$ ) with no evidence of heterogeneity ( $X^2_{(5)} = 8.65$ ,  $p = .12$ ) and with a moderate inconsistency across the studies ( $I^2 = 42.2\%$ ).

This indicates that people with ED take more time in putting pieces of puzzles together to create a familiar object. Although statistically there was no publication bias (Begg's test  $p = .70$ ; Egger's test  $p = .96$ ), the trim-and-fill procedure yielded one filled number showing some evidence of publication bias. A visual inspection of the funnel plot indicated that there is a small publication bias towards larger studies. After correction, the overall effect remained at a moderate level ( $d = 0.35$ ,  $p = .02$ ).

Two studies found that people with AN completed this task faster than controls and the studies were scrutinised for any explanations for this (Galderisi *et al.*, 2003, Thompson, 1993). It is possible that IQ level could be a confounding variable in the study by Thompson (1993). However, the atypical results from the study by Galderisi *et al.* (2003) remain unexplained.

One of the studies reviewed employed a repeated administration of the measures in the same population of early onset of AN after a period of three years (Gillberg *et al.*, 2007). The overall effect size, calculated only for the purpose of providing an estimate and *including* repeated measures, was  $d = 0.42$  (95% IC = -0.66 - 0.19), varying minimally from the results obtained without repeated measures. These results indicate that after three years, when most of the AN group was recovered, persisting difficulties on the OA sub-scale were found in this group (first assessment:  $d = -0.65$ , second assessment:  $d = -0.46$ ).



**Figure 2.7 Forest plot for Object Assembly meta-analysis**  
 (AN ■; BN ▨; Mixed AN ▩ )

### 2.5.3 Co-morbidity

Co-morbid conditions were reported in most of the studies (see Table 2.1).

Some of the studies commented on the effect of co-morbidity on performance in neuropsychological tests. The association between levels of anxiety or depression and task performance is contradictory and inconsistent. The majority of studies found no confounding effects of anxiety (Kingston *et al.*, 1996, Mathias and Kent, 1998, Sherman *et al.*, 2006, Southgate *et al.*, in press, Steinglass *et al.*, 2006) nor of depressed mood (Kingston *et al.*, 1996, Mathias and Kent, 1998, Sherman *et al.*, 2006, Southgate *et al.*, in press, Steinglass *et al.*, 2006, Szmukler *et al.*, 1992). Exceptions were the study by Pendleton-Jones *et al.* (1991), who found a negative relationship between cognitive performance and anxiety, and one study that found a

negative effect of depression on the copy accuracy of the Rey-Osterrieth Complex Figure Test (Thompson, 1993). Obsessive-compulsive symptoms were associated with poor recall in the same task in the latter study (Thompson, 1993).

One study in which 20% of the AN sample met criteria for ASD (Gillberg *et al.*, 1996) observed that this subgroup performed worse in the Object Assembly sub-scale.

Possible confounding effects by medicines were reported in some of the studies. Sherman *et al.* (2006) reported no difference between those taking medicines and those who did not, whereas Kingston and collaborators (1996) found that medicines were associated with poor performance in the Block Design.

## **2.6 Summary**

In general, only a small number of studies have explored aspects of central coherence in the ED literature to date. Most of the studies provide indirect information; none of the reviewed studies directly addressed the hypothesis of weak central coherence. Also, all the studies targeted visual-spatial aspects of cognitive processing only. Therefore there is a lack of information with regards to other domains where a bias towards detail or global processing difficulties would have been demonstrated.

Data were extracted from 15 studies; most of the studies included people with AN and only a few included people with BN. There was a scarcity of studies including fully-recovered samples although some studies included weight recovered and mixed samples. Meta-analyses were conducted for four of the examined tasks obtaining moderate effect sizes across tasks. The Embedded Figures Test had large heterogeneity. Only the most recent study, which reduced the requirement for working memory in performance on the task, showed superior performance in the AN group (Tokley and Kemps, 2007). On the other hand, Object Assembly and Block Design obtained the lowest indices of heterogeneity indicating more consistency between studies' results. Thus, the majority of studies found global processing difficulties across the eating disorder spectrum. Results are less clear regarding local processing.

## 2.7 Discussion

The results from this systematic review are mixed. The findings described above support the hypothesis that posits a decreased function in tests that require a global strategy in ED – e.g. accuracy recall and organizational strategies in the Rey-Osterrieth Complex Figure (RCFT), and Object Assembly (OA) - with moderate effect sizes.

However, the results from tasks that benefit from a more detail focused strategy, such as the Embedded Figures Test (EFT), show marked heterogeneity. The most recent study is consistent with the weak central coherence hypothesis in showing superior function whereas the older studies showed impaired function. Also, the limited research using the Matching Familiar Figures Test (MFFT) showed a relative superior performance in this task by both AN and BN in comparison to HC samples and higher efficiency in the AN group (better speed and accuracy). The case of Block Design (BD) merits further examination. Good performance in this task has usually been interpreted as indicative of superior local processing in people with ASD (Shah and Frith, 1993). In this review, people with ED showed poorer performance on this task with a moderate effect size across the studies. However, there are difficulties in interpreting the results in BD. Although the **superiority** of people with ASD on this task has been explained as an expression of weak central coherence it has been noted that **errors** in this task can also be seen as resulting from weak central coherence. In their recent review of weak central coherence in ASD Happé and Frith (2006) suggest that people with such a bias can fail in this task because they might focus on certain details of the design while excluding others, exaggerating their proportion or relevance in relation to the context. This phenomenon has also been described in other disciplines using similar tasks where more analytical people fail in dividing the whole design in equivalent units (Riding, 2000, Riding and Pearson, 1994). Therefore, a satisfactory trade off between local and global approaches may be involved in successful performance on this task (Strauss et al., 2006). Moreover, the most important element in regards to the weak central coherence hypothesis is the lack of advantage from segmentation of designs. This hypothesis, however, has not yet been tested in the ED field. Taking the results from EFT, MFFT and BD together there is insufficient or conflicting evidence in support of the hypothesis of superior local processing in ED.

### Global and detail processing across the ED spectrum

In general, performance on these global versus local processing targeted tasks across the ED diagnostic spectrum showed little variation. Exceptions were found for the RCFT (recall trial). Difficulties in the RCFT task were consistent amongst AN groups, whereas people with BN obtained more conflicting results in the only two studies included in the review. Murphy *et al.* (2002) found superior performance in the BN relative to the control group whereas Pendleton Jones *et al.* (1991) found no differences between groups. The higher levels of comorbid psychopathology of the BN sample in the latter study in comparison with those who took part in Murphy *et al.*'s study, may account for this difference. Also, it might be possible that those with AN are more consistently impaired on this task due to the poor organisational strategies that affect visual memory, as shown by Sherman *et al.*'s study (Sherman *et al.*, 2006). To our knowledge there is, to date, no study looking at organisational strategies in people with BN. Finally, it is possible that poor nutrition could account for poor performance by the AN samples in this task.

It is noteworthy that the studies of samples of people suffering from BN and of recovered populations focusing on global and local processing are very few which mirrors the general scenario of studies looking at neuropsychological features in people with ED.

To summarise, the weak central coherence hypothesis remains unproved. Evidence of deficits in global processing seems to be consistent across the studies and tasks but, for the main part, superiority in local processing is uncertain because findings from the tasks which were thought to favour a detail focused strategy, e.g. EFT, are inconsistent, or available data are limited (e.g. MFFT) or, as in the case of BD, it is somewhat unclear how to interpret the results.

This contrasts with the conclusion reached by a systematic review of studies examining this hypothesis in ASD (Happé and Frith, 2006). In the latter study there was strong evidence in favour of superiority in local processing but weaker evidence for a deficit in global processing in the ASD population. Therefore, further research specifically aimed at examining whether the difficulties in global processing are accompanied by superiority in detail processing in ED will be needed.



### Study limitations

This review has some limitations. Firstly, none of the studies presented in the review aimed at directly addressing the weak central coherence hypothesis although in two the results were interpreted in light of the weak central coherence account. As a result, the method employed in this review inevitably relied on the indirect extracting of indices of central coherence and is therefore subject to confounding factors (e.g. the working memory component in the EFT). Secondly, the neuropsychological tasks that were examined are associated with local/global processing but also tap into other aspects of executive function and attention which may preclude the specificity of the effect sizes. Thirdly, most of the studies do not provide information on how the measures were administered or whether they have been modified for the particular target population. This makes it difficult to replicate studies, summarise the data and often, to interpret the findings. Likewise, differences in the case or control samples mix such as use of medicines, and diagnostic issues may make it difficult to merge the data.

### Strengths of the study

The present systematic review is an original body of work which adds to the understanding of cognitive functioning of people with ED and reveals some gaps and inconsistencies in the study of cognitive processing, thereby serving as a base for further exploration of this concept. The review followed a two-step search procedure and the QUORUM statement, procedures that helped to systematically search the relevant literature and also avoid the omission of data. Only controlled studies were used which allows for the comparison of the ED results with healthy control samples. It also utilised a meta-analytic approach which is a trustworthy and robust statistical method that enables summarisation and comparison of results across studies and the increase of power of small sample sizes, therefore, the conclusions resulting from such methods are more reliable. Other methodological procedures such as correcting for heterogeneity and publication bias were carried out to provide a more objective evaluation of the available data.

## 2.8 Conclusion

The aim of this review was to summarize the available evidence that could support or refute the hypothesis that people with ED have *weak central coherence* and, wherever possible, to compile a meta-analysis of the results in tasks that differentially involve global or detail cognitive processing styles.

The systematic review showed that people with eating disorders have difficulties in global processing. However, there is less certainty as to whether they have superior local processing. Thus, there is insufficient evidence to refute the weak central coherence hypothesis. More studies that specifically address the weak central coherence hypothesis using appropriate measures are needed. Also, it would be necessary to clarify whether people with ED have superiority in local processing, and to explore the weak central coherence hypothesis in other cognitive domains (e.g. verbal).

The inconclusive but suggesting results from this systematic review set the basis to explore the weak central coherence account in ED further by taking into account the requirements that have been delineated through this review.

## 2.9 The present thesis

The study of cognitive anomalies in the information processing of people with ED opens up a new, somewhat unexplored, area within the examination of factors that may contribute to the aetiology and maintenance of these disorders. We proposed that some characteristics of the information processing of people with ED would represent a vulnerability to the development of the disorders via the underpinning phenotypic manifestations of ED that maintain the disorders such as obsessive-compulsive traits.

Based on the previous revision of the literature and on the evidence in favour of a link between ED and ASD, it seemed possible, but still speculative, to argue that weak central coherence, a cognitive style characterised by a bias toward detail accompanied by difficulties in integrating information into context, was a trait in people with ED which added susceptibility to the disorder.

The aim of this thesis was to advance our understanding of the involvement of the cognitive style of weak central coherence in ED. In order to achieve this overall aim, two objectives were proposed. Firstly, this thesis endeavoured to provide a systematic examination of the concept of central coherence in ED under the conceptual umbrella of the endophenotype approach in psychiatry.

We hypothesised that (1) women with ED in the active phase of the illness, independent of the primary diagnosis, would exhibit a cognitive processing style characterised by weak central coherence, and that (2) weak central coherence would be present also in those who have successfully recovered from the illness. Thus, we aimed to test weak central coherence in light of the first two criteria for an endophenotype for ED.

The method consisted of a series of neuropsychological studies to explore of individual differences in central coherence with the use of a task battery including tests that would primarily benefit from local *or* global processing, measuring two domains of the information processing i.e. verbal and visual-spatial. The test battery was administered to four groups of women (AN, BN, recovered and healthy controls) equivalent in age and intellectual ability. We expected that weak central coherence would be manifested in women with a history of ED in the form of both superiority in capturing details and weaknesses in the ability to integrate pieces of information into a meaningful whole, relative to a healthy control group. Effects of age, level of intellectual ability, duration of illness, co-morbid conditions and recovery status on processing style were examined.

The second objective of this thesis was to demonstrate how findings from neuropsychological explorations could be translated into treatment for ED that target traits of underlying vulnerability rather than the overt phenotypic expressions of the illness. This objective was addressed through the design and implementation of two pilot studies of brief interventions targeting weak central coherence.

In sum, with this thesis I hope to contribute to and further our understanding of the role of anomalies in information processing within the susceptibility for developing ED and how to inform treatment based on findings from neuropsychological studies. Specifically, a systematic examination of the concept of weak central coherence in ED was carried out in light of the endophenotype approach.

## **3 GENERAL METHODOLOGY AND MATERIALS**

### **3.1 Introduction**

The purpose of this chapter is to describe the general methodology of the study of central coherence in women with lifetime eating disorder (ED) in comparison to a healthy control group. This chapter outlines the research design, recruitment and data collection procedures and general methods of analysis. A more detailed description of the samples and specific analyses utilised in the study and of the results it yielded will be presented in Chapters 4 through 9.

### **3.2 Study design**

A cross sectional case-control study design was used in the three studies that assess and compare women with lifetime ED (active and recovered) and healthy controls on neuropsychological performance. A cross sectional design was chosen in this study mainly due to the advantages of reduced costs and increased feasibility in comparison with longitudinal studies especially in rather chronic diseases such as EDs. Cross sectional designs have been questioned particularly for studies including recovered populations. This limitation is addressed in the respective chapter (see Chapter 6).

Only two studies that describe clinical interventions outcomes (Cognitive Remediation Therapy and a brief neuropsychological based feedback intervention) employed a pre-post intervention study design.

### **3.3 Participants**

#### **3.3.1 Power analysis**

The primary outcome measures of this project are the scores from five neuropsychological tests assessing aspects of central coherence. Most of the materials utilised in this project had not been utilised in a population with ED before and/or had been used for different purposes. Therefore, a pilot study with an ED

population was conducted to estimate the sample size required for utilising the five main outcome measures in this project.

Power calculations were conducted using the NQuery 4.0 Advisor program. Based on this pilot study, a sample size of 42 subjects in each group (clinical and healthy control groups) was necessary to have 80% power to detect a clinically significant difference in means of -56 seconds on the Embedded Figure Test (the difference between the AN group mean of 155s. and the HC group mean of 211s) assuming that the common standard deviation was 90 using a two group test with a 0.05 two-tailed significance level. This sample size guaranteed 80% of power to detect medium-large effects for the majority of the neuropsychological tests. Power calculations also indicated that larger sample sizes were required to obtain between group differences of medium effect with 80% power in both the Block Design and Homograph Reading Tests. Such sample size numbers were beyond the scope of this project, however, the aforementioned tests were nevertheless utilised.

### 3.3.2 Inclusion and exclusion criteria for participants

#### **3.3.2.1 *Inclusion and exclusion criteria for all participants***

To be able to participate in the present study participants had to fulfil the following inclusion criteria:

- Women with current diagnosis of anorexia nervosa (AN) aged 16 to 60 years old.
- Women with current diagnosis of bulimia nervosa (BN) aged 16 to 60 years old.
- Women with past history of BN or AN, currently recovered (EDRec).
- Healthy control women (HC) without personal or family history of ED or any other psychiatry disorder and BMI ( $\text{kg/m}^2$ ) between 19 and 26.
- English native speakers or have been living in a country where English was the first language for at least 5 consecutive years and are fluent in English.
- Normal intellectual ability (i.e. estimated intellectual ability from 90 to 110)

Potential participants were excluded as follows:

- Women with current or past history of ED with co-morbid psychiatric psychopathology as their main diagnosis.
- Males: Recruitment was limited to females due to difficulty in recruiting a large sample of male participants in order to control for between group comparisons by gender.
- Women aged below 16 or over 60 years old: Women under 16 were excluded for ethical reasons and women older than 60 years old were excluded to control for possible risk of cognitive deterioration.
- Women with a history of severe head injury, psychosis, epilepsy and/or neurological diseases that may interfere with performance on neuropsychological tasks.

### ***3.3.2.2 Co-morbid conditions and use of medication***

This project did not exclude individuals with ED on the basis of co-morbid psychopathology except if they presented those that were stated as exclusion criteria or if the co-morbid psychiatric diagnosis was their main diagnosis (see above for *Inclusion and exclusion criteria for participants*).

Although depressive, anxiety and obsessive compulsive symptoms may influence cognitive functioning (Castaneda *et al.*, 2008, Kuelz *et al.*, 2004), they all constitute the most common co-morbid conditions in ED (Crane *et al.*, 2007, Halmi *et al.*, 2003, Kaye *et al.*, 2004, Swinbourne and Touyz, 2007, Wildes *et al.*, 2007). These symptoms were assessed in this project and their contribution to performance on neuropsychological tasks was analysed and reported in the corresponding chapters (see Chapters 4 to 9).

Furthermore those with current ED that were taking psychotropic medication at the time of testing were included even though medication could have a confounding effect on neuropsychological performance. Where appropriate, the performance of participants who were on medication was compared to those who were not. Where significant differences in performance were found, analyses were re-conducted excluding the medicated sample.

### ***3.3.2.3 Inclusion and exclusion criteria for those recovered from an eating disorder***

The main criteria to define “Recovered women” included: women who had a history of anorexia nervosa or bulimia nervosa according to DSM-IV criteria but had no remaining symptoms in the current year, with no bingeing, purging, food restriction or excessive exercise according the EATATE interview in the year prior to the study and who had maintained a Body Mass Index (BMI= kg/m<sup>2</sup>) between 19 and 26. Similar criteria have been utilised in previous studies in recovered groups (Matsunaga *et al.*, 2000, Wagner *et al.*, 2006a) and fit with the standard criteria for recovery described by Kordy *et al.* (2002) for both BN and AN. For this study a lenient criterion for recovery in AN was used (i.e. regular menstrual periods were not considered necessary).

## **3.4 Recruitment Procedure**

The recruitment procedure strategy consisted of searching for potential participants using different sources as described below.

### **3.4.1 Recruitment sources**

#### ***3.4.1.1 Clinical Sample:***

Participants with current and past eating disorders were recruited from three different sources. This strategy allowed for the inclusion of individuals from across a broad spectrum of illness severity minimising the likelihood of selection bias towards those more chronically ill.

##### ***3.4.1.1.1 Volunteer Database***

This is volunteer database maintained by the Eating Disorders Unit (EDU) at the Institute of Psychiatry (IoP). This database was built in 1996 and it is available via password access to all researchers working in the EDU. The Unit advertises it on the web-site and people interested in helping with research are offered the registration pack when contacting the Unit. The registration pack includes demographic and clinical questionnaires as baseline information with regards to

lifetime symptom history, in order to help researchers to search for potential participants under specific criteria. It has now amassed a total of 821 volunteers. There is a limitation in using this database to recruit participants for research as those who voluntarily registered as members of the database are essentially a self-selected group and may therefore not represent a 'true' community sample. For this reason, this recruitment strategy was combined with other sources of recruitment.

#### *3.4.1.1.2 Clinical cases of Eating Disorder Units based at the South London & Maudsley Trust*

Women under the care of outpatient eating disorder units at the Maudsley and Guy's Hospitals were approached by the clinical team and invited to participate. Also women in the inpatient unit of the Royal Bethlem Hospital and in the Denbridge House transitional care facility were invited directly by the researcher or via flyers informing about the project.

#### *3.4.1.1.3 Web-site*

A community sample was also recruited using advertisements posted on our web-site ([www.eatingresearch.com](http://www.eatingresearch.com)).

#### *3.4.1.1.4 General Media*

On some occasions representatives of the Eating Disorder Research Unit team have been invited to television programmes or have been interviewed as specialists in the area of ED for newspaper articles, magazines or radio programmes. These occasions provided a great opportunity to advertise the studies being carried out by the Unit. Many patients and carers approached the Unit in response to these advertisements.

The last two sources of recruiting brought more variability of diagnoses and clinical characteristics to the sample as they included generally less severe cases with or without treatment. Also, these strategies were exceptionally important in recruiting volunteers with current BN and recovered women as the former are a group characterised by difficulties in seeking help from professionals (Fairburn and Harrison, 2003) and recovered women are mostly not attending the specialists services.



### **3.4.1.2 Control Sample:**

#### *3.4.1.2.1 Control Database*

Participants were recruited through a bio-track database for healthy control participants. This database contains personal information of potential candidates for research. Where the general demographic data of members of this database matched the inclusion criteria of this project, healthy volunteers were approached by phone by the researcher who informed them about the project and what it involved. This recruiting method was the least successful one for this project.

#### *3.4.1.2.2 Staff and Student Population at the IoP and KCL*

Staff and student participants (undergraduate and postgraduate students) were recruited using emails list circulars approved by the Research Ethics Committee of King's College London. Students and staff voluntarily replied to this circular email which proved to be an effective method of recruiting. One circular to IoP and KCL staff and students asking for healthy and affected volunteers and one to staff and students of KCL looking for affected volunteers were sent in the course of the project.

#### *3.4.1.2.3 Web-site advertisement*

A community sample was also recruited using advertisements posted on our web-site ([www.eatingresearch.com](http://www.eatingresearch.com)), which is usually visited by many affected and unaffected people.

### **3.4.2 Blinding**

As the researcher who collected and analysed the data has also designed the project, it was impossible to be blind to the case/control status of each participant. To minimise researcher bias in the data collection and scoring of outcomes, the following procedures were used:

- The EATATE semi-structured interview is used to confirm ED diagnosis and assess co-morbidity and personality traits. This interview has explicit parameters as to how to conduct the interview and score participants' responses which help to ensure administrator objectivity.

- To guarantee reliability in the data collection and scoring of neuropsychological measures, some measures were video or tape recorded (Rey-Osterrieth Figure Test and verbal tasks) and a proportion (30%) of them were scored in parallel by a researcher blind to the group membership of participants. There were good intra-class correlation coefficients indicating high inter-rater agreement (all higher than .89).

### 3.4.3 Diagnosis and screening

#### ***3.4.3.1 Participants with active eating disorders***

Diagnoses of Anorexia Nervosa and Bulimia Nervosa were made according to the criteria specified in DSM IV (APA, 1994). The EATATE semi-structured interview (part I) (Anderluh *et al.*, 2003) was employed to assess lifetime diagnosis (see description in section 3.5, Demographic and Clinical Measures).

#### ***3.4.3.2 Healthy control participants***

HC were screened for lifetime history of ED using a modified version of Eating Disorders Examination-Questionnaire (Fairburn and Beglin, 1994). For details see **Error! Reference source not found.**

#### ***3.4.3.3 Women recovered from an eating disorder (EDRec)***

Participants in the EDRec group were also assessed with the semi-structured diagnostic interview EATATE encompassing lifetime diagnosis for eating disorders (part I) and comorbid conditions (part II and III) (Anderluh *et al.*, 2003). The EATATE produces a description of eating disorder symptoms over the life course, which in this study helped to determine the status of recovery of participants.

#### 3.4.4 General description of participants<sup>4</sup>

Participants were divided into four different groups each one consisting of:

- Women currently affected by Anorexia Nervosa (AN): This group was composed of 42 women with purging (ANP) or restricting (RAN) AN.
- Women currently affected by Bulimia Nervosa (BN): This group was composed of 42 women with either purging (PBN) or non-purging (NPBN) BN.
- Women recovered from an eating disorder (EDRec): This group was composed of women who were free of eating disorder symptoms for at least one year prior the study, and who were affected by either AN or BN (or both) in the past (see section 3.3.2.3).
- Women who have never had an eating disorder (HC): This group was composed of 42 healthy control volunteers.

Clinical and control samples were matched for demographic variables including age, sex and intellectual ability levels.

### **3.5 Demographic and Clinical Measures**

A broad range of measures was used in this study. Main outcome measures were the neuropsychological tests that comprised the central coherence battery. Secondary outcomes were measures of personality traits and preferences that might be linked to central coherence (measures of obsessive compulsive personality traits and autistic type traits). Below, a description of all the instruments utilised in this study is provided.

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<sup>4</sup> This description refers to the participants who took part in the cross sectional studies of central coherence. Full description of the samples as well as the description of participants who took part in the clinical intervention studies will be described in the corresponding chapters.

### 3.5.1 Demographic questionnaire:

Demographic and general medical history details (e.g. use of medicines, family members with eating disorders, etc.) were obtained using a standard form.

### 3.5.2 Body Mass Index (BMI):

Body Mass Index ( $\text{kg/m}^2$ ) was calculated for all patients at the time of the interview, after which patients were weighed. In 3 cases where weighing meant a major stress for the patient, and in those cases where the participant was admitted in the inpatient unit at Bethlem Hospital, weight was taken either from clinical notes or reported by the patient.

### 3.5.3 Co-morbidity measures

A number of self-report questionnaires were given to all participants to assess levels of symptoms of the most typical co-occurring conditions of ED such as anxiety (Kaye *et al.*, 2004, Swinbourne and Touyz, 2007), depression (Wildes *et al.*, 2007) and obsessive-compulsive disorders (Halimi, 2005). These disorders usually accompany ED, persist after recovery (Gillberg *et al.*, 1995, Holtkamp *et al.*, 2005, von Ranson *et al.*, 1999) and might affect cognitive performance (Castaneda *et al.*, 2008, Kuelz *et al.*, 2004). The selected battery of self-report measures included:

#### **3.5.3.1 *The Hospital Anxiety and Depression Scale – HADS***

The HADS is a brief and well validated 14-item self-report instrument that assesses current symptoms of depression and anxiety using two independent clinical scales (Zigmond and Snaith, 1983). Participants need to complete a questionnaire which is composed of statements relevant to either anxious (e.g. “Worrying thoughts go through my mind”) or depressive (e.g. “I feel as if I am slowed down”) symptoms. Each statement is followed by a 4-point scale (0-3) according to severity of the symptoms (e.g. “not at all”, “occasionally”, “quite often”, “very often”).

The total score is the sum of the individual items scored per scale with possible scores ranging from 0 to 21. Total scores are understood as: 0-7 no clinical significance, 8-10 mild levels of symptoms, 11-15 moderate levels of symptoms and 15-21 severe depressive or anxiety symptoms. A score of 11 or higher on any scale indicates clinical ‘caseness’ of mood disorder. Scores between 8 and 10 suggest the

presence of the respective state (Snaith, 2003). The cut-off of 8 or higher has been found to show the most optimal balance between sensitivity and specificity. Finally, HADS has shown good internal consistency with a mean Cronbach's alpha for HADS-A (anxiety) of .83 and for HADS-D (depression) of .82 (Bjelland *et al.*, 2002).

### **3.5.3.2 *The Obsessive – Compulsive Inventory Revised Version – OCI – R***

The OCI-R self-report questionnaire is a well validated 18-item screening tool for obsessive-compulsive disorders (Foa *et al.*, 2002). This is a short version of the original scale (Foa *et al.*, 1998) and includes six subscales measuring a variety of obsessive-compulsive symptoms such as washing (e.g. "I sometimes have to wash or clean myself simply because I feel contaminated"), checking (e.g. "I repeatedly check doors, windows, drawers, etc."), ordering (e.g. "I get upset if others change the way I have arranged things"), neutralising (e.g. "I feel I have to repeat certain numbers"), hoarding (e.g. "I collect things I don't need"), and obsessing (e.g. "I am upset by unpleasant thoughts that come into my mind against my will"). Participants need to fill in the questionnaire stating whether the described symptom has produced distress in the last month, on a scale from 0 ("not at all") to 4 ("extremely"). Therefore, the total score could range from 0 to 72. A cut off point of 21 has demonstrated the best balance between sensitivity (65.6%) and specificity (63.4%) for the full scale when comparing individuals with OCD and healthy controls. In the case of the subscales a cut off of 4 points has shown to be the most appropriate (sensitivity of 74.4% and specificity of 76.1%) (Foa *et al.*, 2002). The OCI-R has good psychometric properties. The Cronbach's alpha for the full scale ranged from .81 and .93 for four groups tested in the study in which the short OCI was developed. Internal consistency coefficients higher than .72 were found in four out of the six subscales, with the exception of neutralising and checking in non-anxious individuals.

### **3.5.3.3 *The EDE-Q4: A Modified Version of The Eating Disorder Examination-Questionnaire – EDE-Q***

The EDE-Q is a self-report version of the Eating Disorder Examination (Fairburn and Beglin, 1994), the well established investigator-based interview (Fairburn and Cooper, 1993). For this study the EDE-Q was modified to encompass lifetime symptoms (see Appendix A) and utilised as a screening measure for healthy volunteers. This questionnaire explores the presence and frequency in the past of eating behaviours such as restricting, binges (objective and subjective), use of purging behaviours (laxatives, diuretics) and exercises as means of controlling weight and shape. For this purpose, if the potential participant responded to any of the questions positively, the examiner explored the question further to determine if the eating disorder behaviour was still currently present.

### **3.5.3.4 *EATATE LIFE Phenotype***

This is a semi-structured interview designed to measure lifetime history and course of eating disorder symptoms (part I) as well as history of comorbid psychiatric conditions (parts II and III) utilising a biographical approach that elicits detailed diagnostic information, following the DSM-IV criteria (Anderluh *et al.*, 2003). The EATATE was developed by The Healthy Eating Project and it is based on the Eating Disorder Examination interview (EDE: Fairburn and Cooper, 1993), and the Longitudinal Interval Follow-up Evaluation interview (LIFE: Keller *et al.*, 1987) both of which are well established diagnostic tools. The EDE interview has been found to be a valid and reliable instrument for current (Fairburn and Cooper, 1993) and retrospective diagnosis of ED (Ravaldi *et al.*, 2004) and the LIFE interview is a commonly utilised instrument to assess longitudinal course of psychiatric illnesses and has been successfully used in the ED field (Eddy *et al.*, 2008, Herzog *et al.*, 1993, Schmidt *et al.*, 2007).

For this study, the EATATE part I was administered to clinical and recovered participants only. Additionally, parts II and III were administered to all participants (including HC) to examine for a history of other psychiatric problems.

### 3.5.4 Personality traits

It was of most interest to explore the potential relationship between, a) obsessive-compulsive traits, and b) autism spectrum disorder (ASD) type traits, and weak coherence, as they are hypothesised to be underpinned by this cognitive style.

#### 3.5.4.1 The Autistic Spectrum Quotient – AQ

This is a 50-item questionnaire probing autism tendencies in adults (Baron-Cohen *et al.*, 2001). It is composed of five subscales assessing the main diagnostic characteristics of those with ASD: social skills (e.g. ‘I find it hard to make new friends’), attention switching e.g. ‘New situations make me anxious’), communication (e.g. ‘I frequently find that I don’t know how keep a conversation going’), imagination (e.g. ‘I find making up stories easy’, reversed scoring), and attention to detail (e.g. ‘I often notice small sounds when others do not’). Each subscale is composed of 10 items that are scored 1 if the answer endorses either slightly or strongly the abnormal behaviour. Therefore, the maximum score per scale is 10 and the maximum total score is 50. The subscale does not include any control items. The measure has good psychometric properties. In early studies, a cut off point of 32 was reported to correctly diagnose 80% of those with ASD versus only 2% of controls in a community sample (Baron-Cohen *et al.*, 2001). Later, a new cut off of 26 was described as being the most useful for screening purposes in clinical settings. At this cut off score the sensitivity is 0.95, specificity 0.52, positive predictive value 0.84, and negative predictive value 0.78 with 83% of patients being correctly classified (Woodbury-Smith *et al.*, 2005). The AQ has been found to be a reliable and valid measure in studies across different cultures (Baron-Cohen *et al.*, 2001, Hoekstra *et al.*, 2008, Wakabayashi *et al.*, 2007, Woodbury-Smith *et al.*, 2005)

The results of participants’ scores on these personality measures and their relationship with central coherence measures are described in Chapter 7.

### 3.5.5 Intellectual ability

#### 3.5.5.1 *The National Adult Reading Test – NART (Revised)*

This is a widely used valid and accepted measure for estimating pre-morbid intellectual ability in neuropsychological research (Strauss et al., 2006). Two editions of this test have been validated and standardised for British samples (Nelson, 1982, Nelson and Willison, 1991) aged 18 and older. The latest revised edition was utilised in this study. There are a number of advantages and a few disadvantages in using this test. Among the advantages are: good psychometric properties (reliability estimates for internal consistency are above .90, with a test-retest reliability of .98 and above .88 for inter-rater reliability); the test seems unaffected by the influence of the psychiatric disorders which are often co-morbid in samples of ED studies (e.g. depression); performance on the test is thought to be independent of brain damage; it has straightforward administration and scoring procedures; administration takes a short time which is especially important for studies involving a large number of tests; and it is a robust predictor of intelligence in the normal adult population. However, there are some caveats. The NART relies upon the individual's reading ability therefore it cannot be used with individuals with impaired reading ability (e.g. dyslexia). It assumes that the words are familiar to the individuals undertaking the test and therefore it is less useful for individuals where English is not their first language or in different ethnic group. Finally, and it is able to predict only a limited range of IQ (from 75 to 131 for the full IQ scale) (Strauss et al., 2006).

In terms of procedure, NART requires participants to read out loud 50 irregularly spelled words (e.g. leviathan, psalm, façade) from a A4 paper sheet, with different levels of difficulty and irregularity in terms of grapheme-phoneme (symbol-sound) correspondences (Bright *et al.*, 2002). One point is given to each word inaccurately pronounced based on a pronunciation guide and the total errors score is transformed to an estimate of intellectual ability equivalent to the intellectual quotient as measured by WAIS-III. Subtle variations in pronunciation are acceptable when they are caused by different regional accents. This test takes about 10 minutes for full administration.

For this study, participants' answers were tape recorded and scored in comparison to a recording of correct pronunciation by a native speaker to ensure



scoring accuracy, as the principal researcher is not an English native speaker. An additional native speaker also further checked scoring.

### 3.6 The Central Coherence Battery

The battery of tasks intended to measure central coherence (local/detail focused and global integration processing) was assembled in consultation with Dr. Francesca Happé, Reader in Cognitive Neuroscience, and Dr. Rhonda Booth from the Research Centre of the Social, Genetic and Developmental Psychiatry (SGDP) of the Institute of Psychiatry. Dr. Booth did her doctoral thesis on the topic of central coherence in ASD and typical development population under the supervision of Dr. Happé (Booth, 2006). Happé and Booth have recently published an interesting revision of the concept of coherence (Happé and Booth, 2008).

The neuropsychological battery chosen consisted of 5 tasks (see Table 3.1). These tasks were selected to span at least two modalities of processing (visual-spatial and verbal) and the two dimensions of weak central coherence hypothesis: tasks that allow the investigation of either the superiority in detail processing (tasks that implicitly benefit from a predominant local processing) and difficulties in global integration (tasks that benefit from global processing). Tasks that had shown good sensitivity in studies comparing high functioning ASD and healthy controls, or were showing promising results at the time of the consultation were chosen. No tasks looking at predominant detail processing in the auditory/verbal domain were selected.

**Table 3.1 The Central Coherence battery of tasks according to modality and levels of processing.**

	<b>Visual-Spatial Tests</b>	<b>Auditory/Verbal Tests</b>
Predominant Detail Processing	Embedded Figures Test Un/segmented Block Design	None
Predominant Global Processing	Rey-Osterrieth Complex Figure	Sentence Completion Task Homograph Reading Task

As is true for most of the neuropsychological measures, any of the tests selected for this study may be measuring cognitive processes other than central coherence. There are many ways in which performance can be compromised. In order to reduce the potential confounding effect from other cognitive functions, a range of tasks were used and, more importantly, some of the tasks were modified from their standard form. A description of these modifications is presented below along with the individual description of the tasks.

However, it must be acknowledged that in some tasks there is a trade off between detail and global processing and it is difficult to separate the two processes as it is described above. In this study tasks were divided between tasks in which detailed focus processing would benefit performance and tasks in which integrative processing would benefit performance. This theoretical division was tested using statistical procedures, the results of which are presented in Chapter 7.

### 3.6.1 Tasks that benefit from detail focused processing

#### ***3.6.1.1 The Embedded Figures Test***

The Embedded Figure Test (EFT; Witkin et al., 1971) is a perceptual measure commonly employed in neuropsychological studies to explore analytical ability and cognitive styles in a low level of visual-spatial processing modality. It measures the time taken to locate and trace 12 simple shapes embedded in larger and complex non-meaningful designs.

There are different versions of the task. Initially versions for individual administration in adult and children populations were developed. The adult version of the task consists of 24 complex non-meaningful figures and 8 simple figures selected after several validation studies. These items were divided into two equivalent experimental sets (forms A and B). Reliability studies of this task for populations over 16 years old have shown values ranging from .61 and .90. (Witkin et al., 1971). The children's version (Karp and Konstadt, 1963) consists of 25 items that involve finding simple shapes in meaningful designs. Finally, a group version, so called the Group Embedded Figures Test has been developed in which the individual version was adapted to be used in groups (Witkin et al., 2002). It contains a larger

number of practice and experimental items and stimuli are presented in the form of a booklet.

The EFT has been utilised since 1950 (Witkin, 1950) in a variety of fields and has had a profound impact on the development of personality theories that index the competence at disembedding in this test as a manifestation of broader psychological dimensions such as field dependency/independency and psychological differentiation (Witkin et al., 1971). Also, certain psychiatric pathologies have been described as linked to patterns of field dependence/independence as shown by this task. The performance in the EFT is thought to be an enduring mode of the individual's functioning in situations that involve disembedding abilities, beyond the visual-spatial modalities. For this study, the interest is focused on the analytical task that the test involves, therefore, on the assessment of the ability to break up an organised visual background (complex figure) in order to separate a part of it from that background.

In the study of individuals with ASD this task has been one of the core tasks used to explore the hypothesised superiority in detail processing (Happé and Frith, 2006, Jolliffe and Baron-Cohen, 1997, Kaland *et al.*, 2007, Ropar and Mitchell, 2001, Shah and Frith, 1983). It has been argued that successful performance in this task may be interpreted in two ways: as a result of weak integrative processing (focused on details without seeing the global background of the figure) or a strong local processing (superior) ability to resist the whole and focus on detail (Happé and Booth, 2008, Happé and Frith, 2006).

Materials: Form B of the adults' version was utilised in this study. The task is composed of 12 experimental and one practice items. Each experimental item consists of a pair of cards: one target card contains a simple shape (8 different shapes in total identified by letters A to H) and the paired experimental card contains one complex figure (12 in total numbered consecutively in order of test presentation). Some of the target cards are used more than once whereas the experimental cards are only used once. On the back of the experimental cards is written the corresponding number along with the letter of the target card containing the figure which is embedded in the complex design.

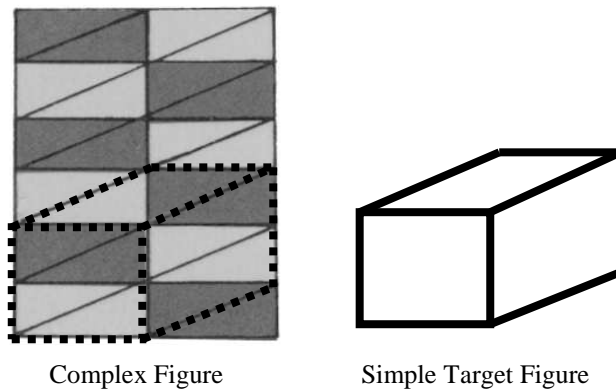
Figure 3.1 shows an example of one of the items. The experimenter manipulates the cards, and administers a scoring sheet, a stopwatch and a stylus pen. The stylus pen is given to the participant to trace the outline of the simple shape

hidden in the complex figure once they have identified it therefore the experimenter can observe the exact point where the participant has identified the hidden simple shape.

Procedure: All participants were offered a standard set of verbal instructions informing them that the experimenter was going to present them with a card showing a simple shape and then a card showing a more complex design wherein the simple shape was hidden. They were instructed that their task was to find and indicate where the simple shape was hidden as soon as they could. They were also informed that more than one simple shape could be in the complex figure but only one was needed. In addition, they were instructed that the simple shape would be embedded in the figure so that it was facing the same direction as the shape they were shown and not rotated in any way.

Time was measured with a hand-held stopwatch, which was started as soon as the complex shape was revealed to the participant and stopped once the participant claimed that they had found the figure. The participant then had to show to the experimenter where in the complex figure they had identified the simple shape, using the stylus pen to indicate the shape. If they were wrong, a 'false claim' was noted, the participant was asked to keep looking and timing was resumed for up to 60 seconds. The practice item was presented first and used to teach the participant the required procedure.

The original procedure has been modified for this study in two ways. In the original procedure, three steps are followed: the experimenter shows the complex design and asks the participant to describe it, then removes the complex figure and shows the simple shape and finally, the experimenter turns the simple shape over and shows the complex design again and asks the participant to find the simple shape. The participant has up to three minutes (180 seconds) to find the embedded figure. If the participant forgot what the simple figure looked like, they could ask the experimenter to show them the target simple shape again. For this study and in order to enhance the importance of a quick response and best effort from participants, the maximum time was decreased to 60 seconds per item. Also, the short-term memory component of the task was omitted by displaying the target and the experimental shapes simultaneously in front of the participant. Therefore, the participant could check the simple figure against the complex design throughout the whole task.



**Figure 3.1** An example of an item from the Embedded Figures Tests

Scoring: Scores are expressed in seconds and represent the median time taken to locate the hidden shapes and number of false claims made during the task. After 60 seconds the item is reported as an “error” and given the maximum score. Thus, the score for each item ranged from 0-60s.

Predictions: The rationale for using the EFT in this study was that it constitutes a reliable measure for speed and accuracy in detail focused processing (superior local processing). A shorter time and fewer false claims suggest stronger detail processing as participants need to ignore the background (context) and focus just on the detail of the shape they are searching for. In this study, the predictions were that those with lifetime eating disorders would be faster and more accurate in finding the hidden figures, especially those who were currently suffering with AN and those that had recovered from AN.

### ***3.6.1.2 The Un/Segmented Block Design Test***

The Block Design Test (BD) is a construction task created by Kohs (1923) and later modified by Wechsler as a fundamental part of the well known battery to measure general intelligence, the Wechsler Intelligence Scale (Wechsler, 1981, 1997). This task has been broadly used as a measure of visual-spatial organisation, non verbal intelligence, psychomotor speed and visual motor coordination ability (Lezak et al., 2004). Indeed, it has been described as the best estimate of ‘g’ (general

intelligence) among the performance tasks of Wechsler sub scale (Lezak et al., 2004). Basically, the test requires the participant to construct replicas of designs increasing in difficulty displayed on a card or computer screen using 4 or 9 wooden coloured blocks.

Kohs highlights the two essential processes required to achieve the solution of this task: analysis and synthesis. Analysis refers to the process of segmenting the whole design into its constituent parts whereas synthesis alludes to the ability to reunite the pieces to form a whole. Shah and Frith (Shah and Frith, 1993) suggested that the analytical process required in this test may favour weak coherence as the whole design presented to the participant needs to be segmented in its parts and reconstructed block by block. Those with weak coherence therefore would automatically segment the whole design in its individual parts. Shah and Frith modified the block design task to test this hypothesis. In this modified version, the task was divided into two modalities of designs: the original un-segmented designs and pre-segmented designs. The hypothesis was that those with weak coherence would have less benefit from the pre-segmentation than those with more global processing due to their natural tendency to see the parts over the whole. The authors probed this hypothesis as people with autism were superior to a matched control group in the un-segmented designs but this effect disappeared in the pre-segmented designs.

Materials: In this study, a modified version of the pre-segmented and segmented block design task was used. Materials included a set of nine yellow and black blocks (2.5 x 2.5 cm) and 11 designs (1 x 2-block practice, 1 x 4-block practice, 4 x 4 –block experimental designs, 1 x 9-block practice and 4 x 9-block experimental designs) to be shown on a 15” computer screen in actual scale. Examples of test items are shown in Figure 3.2.

All blocks were identical, they all had one yellow side, one black side, 2 sides half yellow and half black horizontally divided into equivalent sizes, and 2 sides half yellow and half black diagonally divided into two equivalent halves.

The selected designs were chosen from a range of 31 designs previously piloted by Booth (2006) to match un-segmented (designs were presented as a whole so that the participant needed to break up the design into its component parts to succeed in the task) and pre-segmented (there were divisional gaps in the design between blocks) designs in terms of difficulty.

Finally, a hand held stopwatch to record time and a scoring sheet to record construction errors were used.



**Figure 3.2** Examples of 4-block un-segmented (left) and pre-segmented (right) designs

Procedure: The whole task was divided into two separate sub-tests. The un-segmented part was presented before the segmented to avoid suggesting the use of analytical strategies. Between these two sub-tests, the EATATE semi-structured interview was conducted. Each sub-test commenced with one (or two) practice items. There was also a practice item between the 4 and 9-block parts of the task. The participant was first familiarised with the blocks and was told that their task was to construct replicas of the designs the experimenter was going to show on the computer screen. For the first part, only 4 blocks were needed to copy four designs and the second half of the task required them to use all the 9 blocks. The experimenter then proceeded to show the 4-block practice design and asked the participant to observe how they constructed the replica of the design displayed on the screen. Then, the blocks were scrambled and the participant was required to repeat the process by themselves. If they failed, the 2-blocks practice was presented. Once the participant could successfully construct one practice item, the rest of the sub-test was presented. The participant was asked to work as quickly as they could and was warned that the task was timed. For the 4-block designs a limit on the construction time of 60 s was allowed whereas in the 9-block designs a maximum of 180s was given. If this limit of time of construction was exceeded, it was noted as an error and the participant was advised to leave that item and continue with the following ones.

Scoring: Individuals time and accuracy were scored. Accuracy refers to the number of items completed within the time limit (60s for 4-block items and 180s for 9-block items). Failed items were scored with the maximum time allowed. Since each sub-test is composed by 8 items (4 items of 4 blocks and 4 items of 9 blocks) the median time spent in each section (4 or 9 blocks) was calculated per each sub-test. Total sub-test score (un-segmented or pre-segmented) was calculated by summing up the median time obtained in the 4 and 9-block sections. The relative benefit from segmentation was calculated: total score in un-segmented sub-test minus total score in the pre-segmented sub-test divided by the total score in the un-segmented sub-test. This benefit from segmentation was expressed as a percentage.

Predictions: People with weaker coherence are thought to show less benefit from segmentation and better accuracy (fewer errors). Thus and according the main hypothesis of this study, women with lifetime eating disorders were expected to obtain lower percentage of benefit from segmentation and to make less errors during the task.

### 3.6.2 Tests that benefit from integrative processing

#### **3.6.2.1 *The Rey-Osterrieth Complex Figure***

The Rey-Osterrieth Complex Figure (ROCF) is one of the most broadly used neuropsychological instruments in the neuropsychological exploration created in France by André Rey (Rey, 1941; cited in Strauss et al. 2006, p. 811) and elaborated by Osterrieth (Osterrieth, 1944, Strauss *et al.*, 2006). It is a pen and pencil task that measures a diversity of cognitive processes including: visual perceptual organization, non-verbal memory, planning, problem solving and motor function (Osterrieth, 1944) and it is valid for use in individuals between 6 and 93 years old (Strauss et al., 2006).

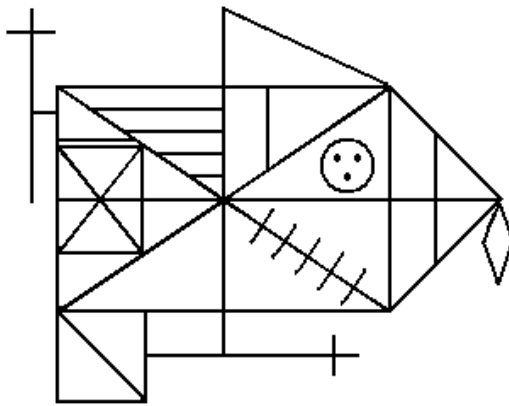
It requires that participants copy and, after a time interval, recall a complex figure (see Figure 3.3). The time interval varies according to the study design. Four basic types of administration procedures have been described: Type A consisting of a copy and a 30-min delayed recall; Type B involving a copy, an immediate recall (right after the copy), and a 30-min delayed recall; Type C which includes a copy and a 3-min recall; and, Type D which requires a copy, a 3-min recall, a 30-min



delayed recall and a recognition sub-test (Strauss et al., 2006). In the present study, administration type A was selected.

There are a number of scoring systems developed to address different aspects of cognitive processing using the Rey Figure (Spreeen and Strauss, 1998, Strauss *et al.*, 2006). In this study the subject of primary interest was the *process* of drawing which may reveal non verbal aspects of coherence through the drawing style utilised by the individual, and secondary, the *accuracy* of drawing. To address the latter, a standard and valid method to score *accuracy* developed by Osterrieth (Osterrieth, 1944) and modified later by Taylor into its current form (Spreeen and Strauss, 1998), was employed. As *process* measures, two developments were chosen amongst a large number of scoring systems for quality of drawing (Lezak *et al.*, 2004, Strauss *et al.*, 2006). Firstly, the *Central Coherence Indices* (Booth, 2006) which were designed to particularly assess central coherence in non verbal tasks, and secondly, a measure for *Organisational Strategy*, thought to be related to executive functioning and developed by Savage and collaborators (Savage et al., 1999). Although not directly relevant for the central coherence hypothesis, the inclusion of the investigation of *Organisational Strategy* was supported by its validity in the study of drawing processing in psychiatric illnesses including eating disorders (Bohne *et al.*, 2005, Deckersbach *et al.*, 2000, Mataix-Cols *et al.*, 2003, Sherman *et al.*, 2006), and its utility in investigating the hypothesised relationship between central coherence account and executive functions.

Materials: Two blank A4 sheets of paper, 10 coloured pencils, a video camera, a score sheet, and the stimulus card depicting the Rey Figure were used. The Rey figure (see Figure 3.3) was reproduced so that the base rectangle, measuring 8 x 5.5 cm, was printed in black and presented on a white A4 card (21 x 29.7 cm) in landscape orientation.



**Figure 3.3 The Rey Complex Figure**

Procedure: In the copy trial, participants were provided with a blank A4 sheet of paper, in the same orientation as the stimulus card, and coloured pencils. When the stimulus card depicting the figure was presented, they were asked to copy the figure as carefully as they could. They also were told that the experimenter would change the pencils as they were drawing and that the process would be video taped.

The experimenter sequentially changed the coloured pencils each time one element of the figure was completed or when the participant moved on to draw another part of the figure. Colours were always given in the following order: black, green, purple, brown, blue, pink, light blue, red, yellow, orange. This method is one of the variants detailed by Lezak to record the procedure (Lezak et al., 2004) and introduces only minimum disruption to the individual's process of drawing (Strauss et al., 2006).

The experimenter instructed the participant to avoid rotating the stimulus card. If the participant said they had made an error in their drawing, the experimenter encouraged the participant to cross it out and then continue. The use of a ruler or an eraser was not permitted. Also, no time limit was imposed on the copy trial (Booth, 2006).

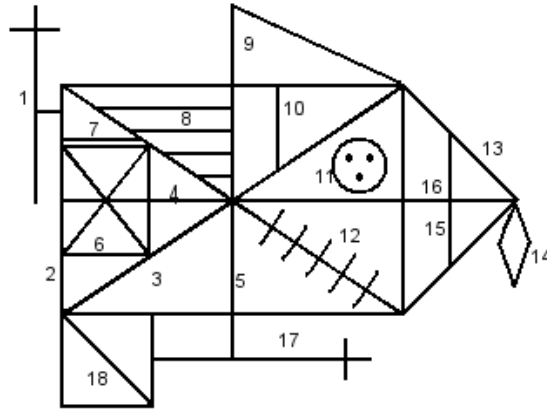
The experimenter gave no prior warning to the participant that a recall trial was required. The session continued with other tests (see 3.8 General procedure) before the recall part of the test was presented. There is evidence that little difference in recall accuracy performance occurs between immediate and delayed recall scores

(Meyers and Meyers, 1995) and that most of the forgetting takes place in the few minutes after the copy (Lezak et al., 2004). Therefore, a unique delayed recall after an interval of 30 minutes (type A administration) was chosen and participants were asked to draw the figure “from memory”. Identical procedures to the copy trial were followed. In addition to the 10 coloured pencils, used in order to enable the identification of order and continuity in which the figure was drawn, a video camera was utilised to record the process of drawing.

#### Scoring:

*Accuracy:* As mentioned before the standard scoring system adapted by Taylor (Spreen and Strauss, 1998, Strauss *et al.*, 2006) was used. This scoring system divides the figure into 18 separate and numbered units (see Figure 3.4), which corresponds with specific details of the figure. These units are scored individually for accuracy and placement and are awarded with scores between 0 to 2 points. Two points are given if the unit is correctly placed and accurately drawn. One point is given if the element was drawn incorrectly but placed correctly; or was accurately drawn but placed incorrectly. Finally, if the element is recognisable, but not drawn or placed correctly, a score of 0.5 is assigned. If the element is omitted no points are awarded. The possible range of accuracy for the copy and recall trials of the Rey figure is 0 to 36. A table detailing the criteria for full scores is given in the **Appendix B**. The intra-class correlation coefficient for inter-rater agreement in accuracy score was .89 with an average *Kappa* coefficient ( $\kappa$ ) of .85, ranging from .72 to .95 for the individual elements, in this study.

Based on *accuracy* scores, the *percentage of recall* (accuracy recall/accuracy copy x 100) was calculated as a measure of memory loss after the interval. This derived measure corrects the recall accuracy score through the copy accuracy score procedure that allows analysing of the effect of quality aspects of the drawing process on the recall of the figure. This score becomes relevant for this study as it has been argued that difficulties in visual memory measured by RCFT could be in part explained by the processing style displayed by the participant during the copy of the figure (Savage et al., 1999).



**Figure 3.4 Elements of the Rey Figure**

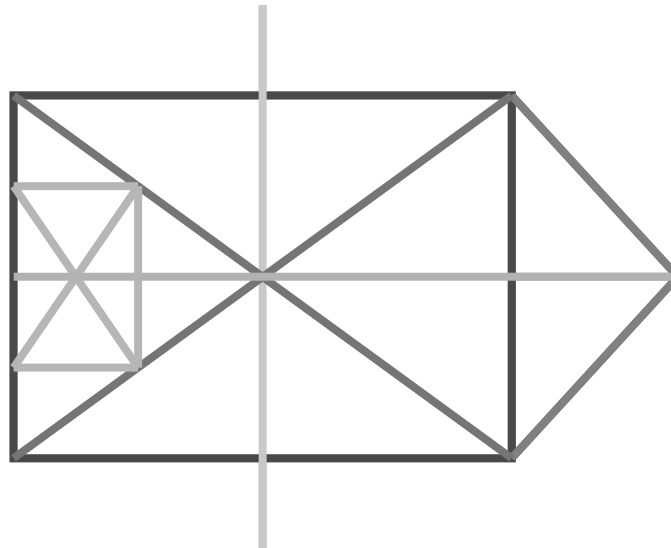
*Central coherence indices:*

Following Booth (2006) the degree of coherence in the drawing process was measured in two independent components:

a) Order of Construction Index: The order of the elements drawn on copy and recall trials was taken from the on-line colour coding recorded by the experimenter and the video record when needed. The outcome of interest was the relative number of global elements as opposed to local elements drawn in the initial stage of construction determined by the first six elements completely drawn. The first six elements were awarded 0 to 4 points according to the following hierarchical categories that reflect the importance of the element to the whole organisation of the figure: (a) a global external structure (elements 2 & 13) = 4 points, (b) a global internal structure (elements 3, 4, 5 & 16) = 3 points, (c) a local perimeter element (elements 1, 9, 14, 17 & 18) = 1 point, and (d) a local internal elements (elements 6, 7, 8, 10, 11, 12 & 15) = 0 points. It is important to note that no score was given to partially drawn elements and that once an element was completed a score was given even if it was constructed with a fragmented style.

The sum of these scores was averaged leading to the *order of construction* index, which could range from 0 to 3.3 points. A higher score is given if the first stage of the drawing involves the global features rather than the detail. Inter-rater correlation coefficient was .93 in this study.

b) Style Index: Six predefined components of the Rey Figure were scored for drawing style, i.e. “degree of continuity” of the drawing process. These components are shown in Figure 3.5, and consisted of the large rectangle (element 2), the diagonal cross (element 3), the extended horizontal line (elements 4 and 16), the extended vertical midline (element 5 plus one segment above or below the rectangle), the sides of the large triangle (element 13), and the small rectangle (element 6). Each of these components were rated on a three-point scale based on the lines of the component present: 2 points were given where lines were drawn in a continuous movement or drawn consecutively, 1 point where the element was partially fragmented or drawn separately (e.g. two non-consecutive movements), and 0 points where the line was clearly disjointed or drawn in a fragmented manner. If the component was absent or not recognisable, no rating was given. The final *style index* was therefore an average of all ratings for components present, and could range from 0 to 2. The sum of these scores is averaged leading to the *style index* which ranges from 0 to 2 points. A higher score indicates more continuity in the drawing style. The intraclass correlation coefficient for the *style index* was .94 in this study with an average *Kappa* coefficient of .89 (ranging from .84 to .96).



**Figure 3.5** Rey Figure: Elements rated for Style (Booth, 2006)

c) Coherence Index: This is a composite score obtained by adding the proportion of the total possible score in *order* (score/3.3) and *style indices* (score/2). The scores could range from 0 to 2. A higher score in the *coherence index* means a more coherent drawing style, i.e. attention and drawing of global elements initially in the drawing process and using a continuous (as opposed to fragmented) style to draw the main elements of the figure. The intra-class correlation coefficient for *central coherence index* was .97 in this study.

*Organisational Strategy*: Drawing style was also assessed using Savage's *et al.* (1999) scoring system for *Organisational Strategy*. A systematic use of organisational strategies is thought to be crucial in encoding and would affect retrieval of new information (e.g. Deckersbach *et al.*, 2000, Grossman *et al.*, 1993, Mataix-Cols *et al.*, 2003, Savage *et al.*, 1999, Savage *et al.*, 2000)

This scoring procedure examines organisational strategies used in the five main components of the figure (elements 2, 3, 4, 5 & 13). In this method, the elements are awarded with 1 point if they are drawn as an unfragmented unit with the exception of element 2 (large rectangle) which, due to its relevance to the fundamental organisation of the figure, is awarded 2 points if unfragmented. Fragmented elements receive 0 points. In case of fragmented units no score is given. The total organisational strategy score therefore ranges from 0 to 6. Higher scores indicate better organisational strategies.

Predictions: The most relevant outcomes for this study were the indices of coherence. It was expected that those with current eating disorders (AN and BN) would have lower scores in the central coherence indices indicating a bias towards detail focused processing over integrative processing. It was also expected that those in the recovered group would be lower in central coherence indices than healthy controls but not as extreme in comparison with those with active eating disorders.

### **3.6.2.2 The Sentence Completion Task**

This verbal test was designed by Happé (2001) to assess global processing in sentences as opposed to the tendency to give locally associative answers when a local cue is offered. The tasks consisted of 25 sentences (for details see

**Appendix C).** Eighteen sentences were constructed to provoke conflict between local and global processing, and 7 without that tension. The version used in this study was modified from the original tasks in consultation with Happé and co-workers. Four of the 15 original sentences (10 experimental items and 5 control items) that were found to be insensitive to differences between affected and healthy control groups or confusing in trials with ASD were removed and 14 new items were added. New items were selected after a pilot study that demonstrated they were valid for the purpose of the task.

In this task, the participant is asked to “finish off” the ending of a pre-recorded sentence, presented on a tape-recorder. Eighteen of the sentences end with a word which is often paired with another, such as “up and...(down)”. This common pairing is a “local” association and in the context of the whole sentence it is incorrect. For example, “In the morning the sun went up and...” the local association “down” is nonsensical whereas “shone all day” is an ending that is correct in the overall global context.

Materials: The 25 sentences were pre-recorded onto a digital machine to standardise the procedure. A computerised audio software was used to record the whole task. The software utilised includes an accurate timer allowing the possibility of recording the length between the end of the pre-recorded sentence and the participant’s response. A record sheet, to record the answer, length of hesitations, number of local completions and final score, was designed.

Procedure: The instructions indicated that the participant was going to listen to some sentences and their task was to “finish off” the sentences. The software started running at the same time as the pre-recorded sentences. The completion can be a whole sentence or a word but the experimenter does not mention this unless the participant asks for specific guidance. Also, the experimenter would try to prevent the participant from repeating the whole sentence when answering and encourage them to provide only a completion. The maximum time allowed for each answer was 20 seconds.

Scoring: Scores are based on participants’ first response. Two aspects of the tasks were scored: a) total score assessing the type of answers (local versus global) as follows: local completions = 2 points; answers given after a delay of 10 seconds, “odd” answers but not clear local completions (i.e. a word local associated to another word in the sentence or a repetition), or no answer = 1 point; meaningful global

completions given within 10 seconds = 0 points, b) total number of local completions (e.g. “salt”...and “pepper”, “up”...and down”, “fish”...and “chips”) used as an indicator of extreme weak coherence.

The intra-class correlation coefficient with a second rater was .99 for total scoring, which is similar to values reported in previous studies (Happé et al., 2001).

Predictions: Higher scores reflect a preference for local processing or difficulties in global processing (Booth, 2006). Therefore a prediction was made that those participants with lifetime eating disorders would have higher scores in the number of local completions and in total scores due to decreased global verbal abilities.

### ***3.6.2.3 The Homograph Reading Test***

This verbal task tests the ability to process a sentence as a meaningful whole rather than on a local level (Happé, 1997). This is a reading task where the participant is asked to read out a set of 16 sentences in which the context of the sentence determines how a homograph (a word that is spelt in the same way as one or more other words but is different in meaning, e.g. the verb 'project' and the noun 'project') within it should be pronounced. Therefore it involves the ability of the participant to ‘spontaneously’ pronounce the sentences taking into account the appropriate context (Jolliffe and Baron-Cohen, 1999). Difficulties in processing words in context are thought to indicate difficulties in verbal coherence (Happé, 1997).

Materials: The sentences were developed by Snowling and Frith (1986), later adapted by Happé (1997) and further modified by Booth (2006). This last version was utilised in this study in which only four of the five homographs from Happé were used (tear, row, lead & bow). In accordance with the adaptation by Booth (2006), a list of 13 pre-test single words that included the 4 homographs was presented on a single A4 page in portrait orientation and the 16 sentences were presented on separate A4 pages, printed in a single landscape orientation line. There were four types of sentences depending on the combination of the position (before or after the context) and the use of pronunciation (rare or frequent) of the 4 homographs (see **Appendix D**). For example: ‘*He took a bow from his music case*’ (target word before context, frequent pronunciation), requires a different pronunciation than ‘*Jack*



*went to speak to the King. Before he began his speech he made a bow* (target word after context, rare pronunciation).

A tape recorder and a scoring sheet including a section in which to note whether the homographs were read in the frequent or rare pronunciation during the pre-test, and a section in which to note the initial pronunciation and whether self-corrections took place for the experimental part of the test, were used. See **Appendix D** for details of the stimuli sentences.

Procedure: The participant was asked to read the pre-test list of words out-loud and the pronunciation was noted. This pre-test was used to check if the participant was familiar with the words. The participant was then requested to read the 16 sentences out-loud, which were presented one after the other in a set order. The whole task was tape-recorded. In the case of errors in the initial pronunciation of the homographs without an attempt at self-correction, a post-test (after the complete task has completed) was administered in order to assess whether the participant was aware of the different meaning and pronunciation of the homograph included in the sentence in which the errors were noted. The post-test consisted of asking the participant whether they knew the meaning of the homographs and whether they knew of any other use and pronunciation of that word.

Scoring: One point was awarded for each sentence read correctly based on participants' initial pronunciation as a measure of context sensitivity (Jolliffe and Baron-Cohen, 1999). For each of the four types of sentences according to the position and the use of pronunciation of the homographs, mean scores (from 0 to 4) were calculated. A total accuracy score ranging from 0 to 16 was derived from the sum of the scores obtained in the four types of sentences. Also, attempts at self-corrections after a wrong initial pronunciation of the homographs were noted. Finally, individual effects of sentence context for initial pronunciation were examined using a difference score across all type of homographs (Booth, 2006) calculated by subtracting the number of correct pronunciations made when the context followed the homograph from the number of correct pronunciations made when the context preceded the homograph.

Predictions: According to the weak central coherence account, participants with a stronger coherence would make more frequent use of the context of the sentences to pronounce the homographs, therefore they would make fewer initial pronunciation errors whereas those with weak coherence would make more errors.

According to Happé (1997) it was also expected that those using the context of the sentences to correctly pronounce the homographs would be more sensitive to their position relative to the sentence context (before or after the context) especially in the rare pronunciation condition. Thus, women with a lifetime eating disorder were expected to make more errors in the initial pronunciation and demonstrate less context effect than the HC group. They were also expected to show a decreased tendency to correct initial pronunciation errors compared to the HC group.

### **3.7 Ethical considerations**

The procedures of this study were approved by the Institute of Psychiatry/ South London and Maudsley NHS Trust Research Ethical Committee (Study number 020/05). Written informed consent was obtained from each participant before participation in this study. Confidentiality of participants was assured at all stages. Participants were allowed to withdraw from the study at any time up to the time their data was coded (thus becoming anonymous) and entered into the database. Participation in the test battery as a whole could take up to three hours, thus participants were offered a reimbursement for their time (£10) and travel costs (up to the value of a day travel card).

### **3.8 General procedure<sup>5</sup>**

All potential participants were administered the screening questionnaire either electronically, via the Internet, or by telephone to ensure they fulfilled the inclusion criteria. In case of doubt, where some of their answers indicated possible difficulties with eating or suggested any other psychiatric disorder, participants were prompted to give more detailed information.

Following a complete description of the study, written informed consent was obtained from all participants by post. In some cases, written consent was obtained on the day of appointment. Those who consented to take part in the research were

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<sup>5</sup> General procedure and Testing procedure described here make reference to the course of action followed for the main studies of this thesis (Chapters 4, 5 and 6). Procedures utilised in studies involving clinical interventions followed particular methods described in the corresponding chapters.

invited to spend approximately two hours with the researcher to complete a neuropsychological battery consisting of six tasks (see below) and to have an interview regarding the lifetime ED (if applicable) during a face-to-face appointment. Participants were also asked to complete a battery of self-report questionnaires on symptoms of anxiety, depression, obsessive-compulsive disorders, and personality traits (see sections 3.5.3 and 3.5.4). An online version of the questionnaires was offered to participants so as they could access them from home. Alternatively, paper versions of questionnaires were either posted before the face-to-face session so they could be handed back on the day of testing, or given on the day of assessment with a prepaid postage return envelope so they could be posted back later. Participants were encouraged to complete the questionnaires within the week before or after the face-to-face assessment so that the questionnaires, especially those assessing anxiety and depression, corresponded to the time of the neuropsychological assessment.

### **3.9 Testing procedure**

All participants were tested individually by the researcher in a quiet room at Guy's Hospital, Institute of Psychiatry or Bethlem Hospital. Participants were given an explanation of the study and of the procedures to be carried out during the session, before the session began. They were informed that the study was aimed at exploring how people think or process different types of information. They were also told about the voluntary nature of their participation, confidentiality, data protection, and that they were able to withdraw their participation at any time up until their data became anonymous and entered into the database.

All participants were administered the battery of tests of central coherence consisting of 5 measures addressing visual-spatial or verbal local-global processing (see section 3.6). In the same session, participants with history of an eating disorder were interviewed in order to assess lifetime history of the illness and co-morbid psychopathology. The HC group was also assessed for psychopathology. Weight and height were measured on the day of testing.

The order of tests and interview administration was as follows: The National Adult Reading Test - NART, The Rey Osterrieth Complex Figure Test (copy trial), the Sentences Completion Task, the Embedded Figures Test, The Homograph

Reading Test, the Rey Osterrieth Complex Figure Test (recall trial), the Unsegmented Block Design Task, the first part of EATATE interview, the Segmented Block Design Test and the final part of the EATATE interview. This order was chosen in order to allow variety between visual-spatial and verbal domains and leave time gaps for those tasks that were divided in two parts (Rey-Osterrieth Complex Figure and Block Design). The session lasted about 2 hours for ED participants and 1 hour and half for those in the HC group. Participants were allowed to have a break if needed after the recall trial of the Rey-Osterrieth Complex Figure.

A general oral feedback about the participant's cognitive style according to their performance on the tasks was given after the session.

### **3.10 General data analysis**

Rigorous statistical procedures were applied following the advice of a statistician, Dr. Daniel Stahl who is a Lecturer in the Department of Computing and Biostatistics at the Institute of Psychiatry.

In order to reduce the risk of type I statistical error without limiting the probability to detect significant findings, the level of  $p < 0.05$  was used to report significant results. To decrease the risk of type II statistical error sample sizes have been determined in order to obtain 80% of statistical power to detect a clinical important effect.

Statistical analyses: The following procedures were conducted for each study in this project unless specific analyses are referred to in the pertaining research chapters:

- Exploratory analyses were conducted to determine whether parametric or non-parametric statistical test were appropriate, looking at standard normality tests and distributions in the histograms for each variable in each group.

- Demographic and clinical data from clinical and control groups were analysed with *t-tests* or ANOVAs.

- Initial between group analyses were conducted using univariate analyses. Independent sample *t-tests* were used for group comparisons and means (*M*) and standard deviations (*SD*) are reported. For those measures without a normal distribution of the data, non-parametric Mann-Whitney *U* tests were used and

medians (*Mdn*) and 25% and 75% quartiles (*Q*) are reported. In case of categorical variables, *chi-square tests* and *Fisher's Exact Test* were carried out.

- Then, between groups analyses for different neuropsychological dimensions, were conducted using ANOVAs (or Kruskal-Wallis). Post hoc tests determined which groups differ where appropriate.

- To explore the relationship between neuropsychological, demographic and clinical variables, explorative Pearson's correlation coefficient (*r*) was used for normally distributed data and linear relationship between the two variables, and Spearman's rank (*r<sub>s</sub>*) correlation was used otherwise. All correlation analyses were conducted separately in each group. Also ANCOVA were carried out in order to investigate the contribution of potential confounding variables on cognitive performance.

-A series of regression analyses were used to examine mediating/moderating effects on a number of outcomes (Baron and Kenny, 1986, Kenny *et al.*, 1998). We present standardized beta regression coefficients (*st.β*) for a comparison of the effects of independent variables with a different measurement range of observations. The assumptions of linear regression models (normality, linearity, independence of residuals) were assessed by a visual inspection of the residuals (Tabachnick and Fidell, 2001). The amount of mediation (indirect effect) was tested using the Sobel test (Sobel, 1982).

-*Cohen's d* was calculated to obtain the effect size for each variable. For those variables with non-normally distributed data, *d* was calculated by transforming the effect-size correlation  $r = \frac{Z}{\sqrt{N}}$  (from Rosenthal, 1991) in *d* using an effect size calculator.

- As this was a novel study, two-tailed tests were used throughout. Hochberg's improved Bonferroni correction for multiple testing was applied on the main outcome measures (Hochberg, 1988). Adjusted and unadjusted p-values are shown.

- Inter-rater reliability analysis was conducted for RCFT by scoring a random selection of 30% of the sample. These cases were investigated using kappa coefficients and interclass correlation coefficient according to the characteristics of the data.

Statistical analyses were in the main conducted using the Statistical Package for Social Science, version 13.0 and 15.0 for Windows (SPSS, Inc., Chicago, Illinois).

## **4 AN EXAMINATION OF CENTRAL COHERENCE IN WOMEN WITH ANOREXIA NERVOSA <sup>6</sup>**

### **4.1 Introduction to the Chapter**

This chapter describes the first experimental study of this thesis, which explored the concept of central coherence in women with a current diagnosis of anorexia nervosa (AN).

For this thesis, this is the key first step towards investigating weak central coherence as an endophenotype for eating disorders as it is aimed at testing the hypothesis of whether people with acute AN do present this processing style. Support for this hypothesis through the results of this study will determine whether the exploration of central coherence merits continuation across ED disorder diagnosis and in the recovery state (Gottesman and Gould, 2003).

### **4.2 Background and Development of the Study**

As mentioned in Chapter 2, the concept of central coherence is relatively new in the field of eating disorders (ED). It has attained an increasing interest in the recent years as a result of both a growing focus on understanding the neurobiology and cognitive functioning of people with AN (Dobson and Dozoi, 2004) in order to inform aetiological models and novel treatment strategies (Lopez *et al.*, 2008a, Schmidt and Treasure, 2006, Tchanturia *et al.*, 2007a), and the initial but promising evidence of a possible link between autistic spectrum disorders (ASD) and ED in cognitive (Gillberg, 1983, Gillberg *et al.*, 2007), developmental (Wentz *et al.*, 2005), personality (Gillberg *et al.*, 1995, Rastam *et al.*, 1997), and social cognitive characteristics (Zucker *et al.*, 2007).

A systematic review of the literature (see Chapter 2) has shown insufficient evidence to fully support the weak central coherence hypothesis in AN. Only two

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<sup>6</sup> A version of this chapter has been published as a research article in the International Journal of Eating Disorders as ‘An examination of the concept of central coherence in women with anorexia nervosa’ (2008: 41: 143-152)

studies prior to the one described in this chapter had mentioned this construct with regards to AN but none of them were intended at extensively investigating this hypothesis (Gillberg *et al.*, 2007, Southgate *et al.*, 2007).

The evidence to date according to the above mentioned systematic review suggests that global integration difficulties, especially in visual-spatial tasks, seem to be consistent and also become apparent in clinical observations revealing the impairment in the ability to see the 'bigger picture' in day to day life (Kemps *et al.*, 2007). The proof with regards the superiority for detail processing purported to be characteristic of people with weak central coherence, is however, somewhat inconsistent. Only two previous studies gave some evidence of this enhanced ability in women with AN (Southgate *et al.*, 2007, Tokley and Kemps, 2007) whereas most of the investigations provide evidence against it i.e. women with AN were slower in tasks involving detail processing (Basseches and Karp, 1984, Pendleton Jones *et al.*, 1991).

However, a narrow cognitive processing and difficulties in abstract thinking, both of which might be explained by a weak coherence, have also been previously described in AN (Gillberg *et al.*, 2007, Strupp *et al.*, 1986, Tokley and Kemps, 2007). Moreover, poor organisational strategies which are thought to be part of executive functioning, were found in women with AN in a study replicating preceding research in obsessive-compulsive disorders, indicating a detailed processing style in response to complex visual information (Sherman *et al.*, 2006). Furthermore, this evidence reinforces commonalities with other disorders with a strong anxiety component such as obsessive-compulsive, body dimorphic and trichotilomania disorders (Bohne *et al.*, 2005, Deckersbach *et al.*, 2000, Savage *et al.*, 1999).

Therefore, as available evidence in the examination of cognitive coherence was insufficient and somewhat inconsistent particularly for superior detail processing, further exploration was required in order to formulate a sound conclusion.



### 4.3 Aims

The present study had the objective of shedding light on the cognitive processing of AN by providing evidence regarding the weak coherence hypothesis in this group. Thus the aim of this study was to measure coherence in people with current diagnosis of AN using a selected battery of tests containing some of the tasks reported in the extensive literature of coherence in the ASD population (Happé and Frith, 2006).

### 4.4 Methods

#### 4.4.1 Study design:

This was a cross sectional case-control study.

#### 4.4.2 Participants:

As described in Chapter 3, 42 women meeting the DSM-IV criteria for AN and 42 healthy controls (HC) matched for sex, age and intellectual ability, took part in this study. A general description of the samples is given below. Full demographics are described later in the chapter (see section 4.6.1).

##### **4.4.2.1 *Participants with current diagnosis of Anorexia Nervosa:***

Participants with AN were ascertained from the volunteer database maintained by the Eating Disorders Research Unit ( $n = 7$ , 16.7%), clinical cases from the eating disorders units based at the South London & Maudsley NHS Trust (Maudsley & Guy's Hospitals Outpatient clinics:  $n = 10$ , 23.8%; Tyson II inpatient unit and day-care unit of Bethlem Hospital:  $n = 11$ , 26.2%); and transitional inpatient care at Denbridge House:  $n = 2$ , 2.4%), and student population of the King's College London ( $N = 1$ , 2.4%). A community sample was also recruited using advertisements on our web-site ( $n = 11$ , 26.2%) (see Chapter 3 for details about Recruitment Sources).

Diagnosis of AN was made according to the criteria specified in the DSM IV (APA, 1994) based on the data obtained using the EATATE semi-structured interview (Anderluh *et al.*, 2003). The distribution in terms of sub-type categories

was as follows: 29 (69%) had AN restricting subtype and 13 (31%) had binge-purge subtype of AN.

#### **4.4.2.2 Healthy control participants**

Healthy volunteers were screened for exclusion criteria using a standard form and for lifetime eating disorders using the modified version of the EDE-Q (Fairburn and Beglin, 1994). Exclusion criteria are described in full in Chapter 3.

Five potential participants were excluded for indicating a history of eating disorder not otherwise specified (EDNOS) and two for having a first-degree relative with psychiatric diagnosis at the time of the screening. Two participants who took part in the study were later excluded as during the diagnostic interview information was given to suggest the possible presence of EDNOS and a bipolar disorder, respectively, which was not mentioned before.

The final group entered in the study was recruited from the staff ( $n = 18$ , 42.9%) and student population ( $n = 14$ , 33.3%) of the Institute of Psychiatry and King's College of London and from advertisements on the Eating Disorders Unit website and local community ( $n = 10$ , 23.8%).

#### **4.4.3 Measures**

A full description of the measures utilised in this study were provided in Chapter 3.

In summary, for diagnosis of eating disorders the *semi-structured diagnostic interview EATATE* for ED (part I) (Anderluh *et al.*, 2003) was used. HC completed the modified *Eating Disorder Examination–Questionnaire* (EDE-Q, Fairburn and Beglin, 1994). Additionally, parts II and III of *EATATE* interview were administered to all participants to examine for a history of other psychiatric problems.

The neuropsychological battery consisted of several paradigms assessing both visual perceptual and verbal coherence. These tests were: *The Embedded Figures Test – form B (EFT)* (Witkin *et al.*, 1971) and the *Un-Segmented/Segmented Block Design Test (Un/seg BD)* (Shah and Frith, 1993) as measures of speed and accuracy in local processing; *The Rey-Osterrieth Complex Figure Test – recall form (RCFT)* (Osterrieth, 1944) to measure visual spatial coherence (Booth, 2006) and

organisational strategies (Sherman et al., 2006); and *The Sentence Completion Task (SCT)* (Happé et al., 2001) and *The Homograph Reading Task (HRT)* (Happé, 1997, Jolliffe and Baron-Cohen, 1999) as measures of verbal tasks with a conflict between local and global processing.

Participants also completed the National Adult Reading Test (NART; 2nd edition) to provide an estimate of pre-morbid intellectual ability based on verbal abilities (Nelson and Willison, 1991), the Hospital Anxiety and Depression Inventory (HADS; Zigmond and Snaith, 1983) and the Obsessive Compulsive Inventory-Revised (OCI-R; Foa et al., 1998) to assess current anxiety, depressive and obsessive-compulsive symptoms.

#### 4.4.4 Procedure

In most cases, weight and height were measured on the day of testing by the researcher. Exceptions were inpatients at Bethlem hospital whose BMI were obtained from clinical notes and two women with AN who reported their BMI themselves as the request to weigh them caused them distress. Both participants looked visibly emaciated.

The NART test was not administered to the first 20 participants as the NART was later added to the protocol. No major intellectual differences were expected between these 20 first participants (five AN and 15 HC) as they were recruited from the same sources as the rest of the sample.

Three women from the AN group and one HC did not return all or part of the questionnaires. Their data were included in the analyses of the main outcome measures. Apart from these four cases, the procedures described in Chapter 3 were followed without exception.

#### 4.4.5 Data Analysis

General procedures for analysis of data defined in chapter 5 were followed. Normality tests (Shapiro-Wilk Test) and visual inspection of histograms of continuous variables revealed that some of the outcome variables' distributions violated the assumption of normality. These were the Sentence Completion and

Homograph Reading Tasks outcomes; time, errors and false claims in the Embedded Figure Test; Un/segmented Block Design Test results; years of education, depression (HADS); and obsessive-compulsive symptoms scores (OCI-R). Therefore non-parametric Mann-Whitney *U* tests were used and medians (*Mdn*) and 25% and 75% quartiles (*Q*) reported. Parametric independent sample *t*-tests were otherwise used and means (*M*) and standard deviations (*SD*) are reported. Additionally, Kruskal-Wallis tests were performed on the mean score for the four conditions of the Homograph Reading Test. Effect sizes were calculated for each outcome measure.

To explore the relationship between neuropsychological, demographic and clinical variables, Pearson's (*r*) and Spearman's rank (*r<sub>s</sub>*) correlation coefficients were used according to the distribution of the data. All correlation analyses were conducted separately in each group and only significant results are described below. When a strong and a significant correlation was found between a neuropsychological and a demographic/clinical variable in which groups differ, the potential effect of the covariate was investigated using ANCOVAs provided that the assumptions associated with this type of analysis were not violated.

Kruskal-Wallis tests were used for between groups comparison after splitting the AN group into its two sub-type diagnostic categories.

It was of interest to measure the processes involved in the RCFT. Sherman and colleagues (2006) have argued that the poor visual memory performance in AN could be partly explained by an anomaly in organisational strategies. Therefore a series of regression analyses were used to examine mediating/moderating effects of *organisational strategy, order, style and coherence indices* on recall in the RCFT (Baron and Kenny, 1986, Kenny *et al.*, 1998). Group was entered as an independent dummy-coded variable, percentage of recall as the dependent variable and central coherence indices as well as organisational strategies score as the potential mediators. Standardized beta (*st.β*) coefficients are presented that allow for a comparison of the effects of independent variables in regressions with a different measurement range of observations. The assumptions of the linear regression models were assessed by a visual inspection of the residuals (Tabachnick and Fidell, 2001). First, Sherman *et al.*'s study was replicated and second, an adapted hypothesis (i.e. to examine whether central coherence indices could also explain poor visual memory) was tested.

## 4.5 Hypotheses and Predictions

The main hypothesis was that people with a current diagnosis of AN would display a local processing bias and weaknesses in global processing in comparison to a healthy control group; in other words, they would show *weak central coherence*.

### 4.5.1 Central coherence predictions on specific neuropsychological performance

According to the weak coherence hypothesis, the following predictions with regards to the performance of the AN group in each of the tasks in comparison to the HC group were made:

- Women with AN would be faster and more accurate (fewer errors and false claims) in tasks that would benefit from detail focused processing such as the EFT and BD.
- Women with AN would benefit less from pre-segmented designs in the Un/seg BD as they would automatically segment the designs into their constituent parts.
- Women with AN would display a more fragmented and focused in detail drawing style in the RCFT (lower scores in central coherence indices).
- Women with AN would show more difficulties in processing sentences in context (SCT and HRT). Therefore, they would make more local associations and would take longer to give appropriate answers in the SCT, and would make more errors in the initial pronunciation of the homographs in the HRT.

An important finding in ASD literature is the aetiological genetic independency of the classical symptom groups of autism (social impairments, communication impairments and restricted repetitive behaviors and interests). Thus the verbal communication deficits in autism and the compulsive symptoms have distinct causal pathways (Ronald et al., 2006). People with AN might therefore only have some of the symptom clusters in common with ASD. For example, they may be more akin to high functioning Aspergers and have fewer verbal difficulties. Therefore, a secondary hypothesis was that deficits in global processing would be most pronounced in the visual-spatial domain rather than in the verbal domain.

Also, it was expected that the restricting type of AN (RAN) and binge-purge type of AN (BPAN) would overall display similar cognitive profiles, as they would share the general endophenotypic characteristics of detail bias. However these two sub-groups would differ from each other in that those with BPAN would show a more impulsive cognitive style (less accuracy) and a better degree of coherence than those with RAN since the former would perform more alike to the functioning described in people with bulimia nervosa (BN) (see Chapter 3 for details and also: Kaye *et al.*, 1995, Toner *et al.*, 1987).

Subsidiary hypotheses were related to performance in other coherence aspects of the tasks:

- Women with AN would recall fewer elements of the RCFT showing poorer non-verbal memory as shown in previous studies using this task (see Chapter 3 for details).
- Group differences in percentage of recall in the RCFT would be partly mediated by drawing style, replicating the observations made in Sherman *et al.*'s study (2006).

## 4.6 Results

### 4.6.1 Demographic and clinical characteristics

The results of general demographic and clinical characteristics are shown in Table 4.1.

People with AN have fewer years of education than the HC group (Mann-Whitney  $U = 558.5$ ,  $p = .01$ ) despite having equivalent levels of estimated intellectual ability ( $t = .40$ ,  $p = .65$ ).

**Table 4.1 Demographic and clinical characteristics of AN and HC groups**

	n		AN	HC	Test statistic		p-value	Effect Size ( <i>d</i> )
	AN	HC			t-test <sup>a</sup>	MW <sup>b</sup>		
Age (years) <sup>a</sup>	42	42	28.4 (9.6)	26.3 (6.4)	.5	n.a.	.58	.26
Number years of education <sup>b</sup>	39	42	15 (12-18)	17 (14.7-19)	n.a.	558.5	.01	-.56
Estimated Intellectual ability <sup>a</sup>	37	27	112.8 (6.8)	112.2 (5.4)	.4	n.a.	.65	.09
BMI <sup>a</sup>	42	42	15.8 (1.7)	21.9 (2.7)	7.8	n.a.	<.001	-2.70
Anxiety HADS <sup>a</sup>	39	41	14.2 (4.6)	6.0 (3.2)	9.4	n.a.	<.001	2.07
Depression HADS <sup>b</sup>	39	41	10.0 (6-14)	2.0 (1-3)	n.a.	115.0	<.001	2.20
OCI-R <sup>b</sup>	39	42	28.0 (16-38)	6.5 (3-10)	n.a.	165.0	<.001	1.90

<sup>a</sup> *t*-test= test statistics for *t*-test pairwise comparisons for data normally distributed, mean values displayed with standard deviations.

<sup>b</sup> MW= test statistics for Mann-Whitney *U* for data not normally distributed, median values displayed with upper and lower quartiles.

na = not applicable.

The anorexia nervosa group had had a prolonged illness ( $M = 13.1$  years,  $SD = 11.2$ ) with profound emaciation and high levels of depressive, anxiety and obsessive-compulsive symptoms. The mean age of onset for the AN group was 15.7 years ( $SD = 4.0$ ). Also, 17 (40.5%) were taking psychoactive medication (58.8% SSRI antidepressants) and 15 (35.7%) were undergoing inpatient treatment at the time of the study. A total of 23 AN participants (54.8%) had received inpatient treatment. All significant results displayed in Table 4.1 remained significant after Hochberg's improved Bonferroni correction for multiple testing (Hochberg, 1988) at  $p < .05$ .

It is important to notice that anxiety, depression and obsessive-compulsive symptoms were measured in terms of level of severity and they do not indicate a clinical diagnosis.

#### 4.6.2 Neuropsychological function

The results from tasks thought to benefit from detail processing are displayed in Table 4.2 and further description by task is given below.

**Table 4.2 Neuropsychological tasks that benefit from a detail focused processing**

	AN n=42	HC n=42	Test statistic t-test	MW	p-value	Effect Size ( <i>d</i> )
EFT total time taken (medians) <sup>b</sup>	8.6 (5.8-13.9)	12.2 (7.9-15.3)	n.a.	639.0	.03	-.50
EFT number time out failures <sup>b</sup>	0.0 (0-1)	1 (0-2)	n.a.	525.0	.001 <sup>c</sup>	-.82
EFT false claims <sup>b</sup>	1 (0-1.3)	2 (0-3)	n.a.	610.0	.01 <sup>d</sup>	-.58
Un-segmented Block Design <sup>b</sup>	52.1 (39.5- 76.2)	44.9 (36.5-62.7)	n.a.	777.0	.35	.20
Segmented Block Design <sup>b</sup>	30.9 (26.6-37.0)	27.7 (25.5-31.5)	n.a.	643.0	.03	.47
Benefit from Segmentation <sup>a</sup>	41.3 % (17.0)	40.9 % (16.3)	-.108	n.a.	.91	.02

Note: Legends as previous table

<sup>c</sup> = Results that remained significant ( $p < 0.05$ ) after Hochberg correction for multiple testing (Hochberg, 1988). <sup>d</sup> = Results dropped to trend levels ( $p = .07$ )

##### **4.6.2.1 *Embedded Figures Test***

Participants with AN excelled in this task as they were able to identify the hidden figures faster and completed more items within the time limit than the HC group. They also made fewer false claims during the task, demonstrating better accuracy.



#### 4.6.2.2 *Un-Segmented Block Design Task*

Women with AN performed slower than HC in the pre-segmented block design sub-test. No significant differences however were found in the un-segmented sub-test or in accuracy. More importantly, groups were equivalent in terms of benefit from segmentation of designs.

The following are the results from tasks that might benefit from global processing. Details of these results are displayed in Table 4.3.

#### 4.6.2.3 *Rey-Osterrieth Complex Figure Test*

The AN group obtained lower scores on all central coherence indices (order, style and coherence indices) of the RCFT in comparison with the HC group. Overall, these results indicate that people with AN displayed a more detailed focus and fragmented drawing style than the HC group.

**Table 4.3 Neuropsychological tasks that benefit from global integration**

		AN n=42	HC n=42	Test statistic		p-value	Effect Size ( <i>d</i> )
				t-test	MW		
RCFT	order <sup>a</sup>	2.1 (0.6)	2.5 (0.4)	3.9	Na	<.001 <sup>c</sup>	-.89
	style <sup>a</sup>	1.3 (0.5)	1.7 (0.3)	2.3	Na	.001 <sup>c</sup>	-.98
	coherence <sup>a</sup>	1.3 (0.4)	1.6 (0.3)	4.1	Na	<.001 <sup>c</sup>	-.93
SCT local processing score <sup>b</sup>		1.0 (0-2)	0 (0-1)	na	591.5	.004 <sup>c</sup>	.65
SCT number of local completions <sup>b</sup>		0 (0-0)	0 (0-0)	na	839.5	.53	.14
HRT total score <sup>b</sup>		15 (14-16)	15 (14-16)	na	877.5	.97	0

Note: Legends as previous table

<sup>c</sup> = Results that remained significant ( $p < 0.05$ ) after Hochberg correction for multiple testing (Hochberg, 1988).

#### **4.6.2.4 Sentence Completion Task**

The AN group obtained a higher local processing score mainly due to a longer time of hesitation before producing an appropriate completion of the sentences. However, the frequency of local completions made by either group was rare. In order to better explore the differences between groups in this task due to the small variance in the results, the procedure described by Happé and collaborators (2001) was followed. Participants were divided into groups showing good and poor performance. An individual met the criteria for a poor performance if they had either one or more local completions, or two or more long hesitations. Thus, 35.7% of the AN group fell in the poor performance group whereas only 16.7% of the HC fell in that category (*Fisher's Exact Test* = .08).

#### **4.6.2.5 Homograph Reading Task**

Overall, performance was equivalent between groups (see Table 4.3). None of the participants showed difficulties reading the homograph from the pre-test list out loud. No differences were found in both the total initial pronunciation score and across the four homograph conditions (all  $p > .44$ ). Also, groups were alike in the number of individuals within groups that made any errors in the initial pronunciation of the homographs ( $\chi^2 = .05, p = .83$ ). Interestingly, a higher percentage of people in the AN group made self-corrections (AN = 37,5% versus HC = 16%) although this difference failed to reach formal significance ( $\chi^2 = 2.90, p = .09$ ). An examination of the effect of context position was carried out using Wilcoxon's Signed Ranks Tests within each group for rare and frequent pronunciation conditions. Individuals with weak coherence were expected to show less sensitivity to the position of the homograph relative to the sentence context (before or after context). However, both groups improved their performance when context preceded the target homograph. This within group advantage was statistically significant only for the rare type of homographs (HC:  $z = -2.18, p = 0.3$ ; AN:  $z = -3.22, p = .001$ ). Finally, individual effects of sentence context for initial pronunciation were examined using the difference score across all type of homographs (the number of correct pronunciations after context minus the number of correct pronunciations before context). No differences between the AN and HC groups were found in the difference score in

either rare or frequent conditions and in the overall difference score (all Mann-Whitney  $U > 815.5$  and  $p > .52$ ,  $d < .15$ ).

As shown in Table 4.3 all significant results remained significant after correction for multiple testing.

#### 4.6.2.6 Additional aspects of cognitive performance

Supplementary information about cognitive functioning was obtained from the performance on the Rey Osterrieth Complex Figure test and is displayed on Table 4.4. Both AN and HC groups were comparable with regards to the accuracy in copying of the complex figure. However, they differed in terms of non-verbal strategic memory (recall accuracy). The AN group recalled less of the figure in absolute terms and also after correcting by copy accuracy (percentage of recall).

**Table 4.4 Accuracy and organisational strategies in RCFT**

	AN <i>n</i> =42	HC <i>n</i> =42	Test statistic		<i>p</i> -value	Effect Size ( <i>d</i> )
			t-test	MW		
RCFT copy accuracy <sup>a</sup>	30.9 (3.0)	30.9 (3.6)	.33	n.a.	.97	0
RCFT recall accuracy <sup>a</sup>	16.7 (5.6)	19.6 (5.7)	2.3	n.a.	.02	-.52
RCFT percentage of recall <sup>a</sup>	53.7 (16.1)	62.8 (15.8)	2.6	n.a.	.01	-.58
Organisational Strategy <sup>b</sup>	4 (2-5)	5 (3-6)	n.a.	552.5	.003	-.70

Note: Legends as previous table

All significant results remained significant ( $p < 0.05$ ) after Hochberg correction for multiple testing (Hochberg, 1988).

Finally, organisational strategies during the copy trial, a component of executive functioning which involves planning and organisation of the drawing process, was found to be significantly impaired in people with AN.

Since organisational strategies and central coherence indices are quality process measures for the copy of the RCFT, the relationship between these two concepts was investigated further. A marked degree of correlation between the two

main process measures, i.e. general coherence index and organisational strategies, was found in this study ( $r_s = .77, p < .001$ ).

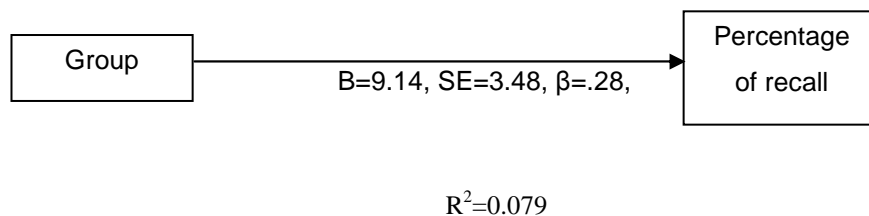
#### 4.6.2.7 *The role of drawing style on visual memory seen in the RCFT*

Following Sherman and colleagues' study (Sherman et al., 2006), a series of regression analyses were conducted to first replicate their findings and then to test the hypothesis of a mediation effect of central coherence on non-verbal memory (see 4.4.5, Data Analysis).

Therefore, two separate mediation hypotheses were probed using organisational strategies and the novel coherence indices following Kenny *et al.*'s procedures for mediation analysis (Kenny et al., 1998).

The hypothesis that some of the group difference in visual memory (percentage of recall) could be partly explained by the use of poor coherence or organisational strategies was supported.

Simple regressions showed that the "Group" variable accounted for 7.9% of the overall variance ( $B = 9.14, SE = 3.5, st.\beta = .28, t = 2.63, p = .01$ ) in percentage of recall (see Figure 4.1).



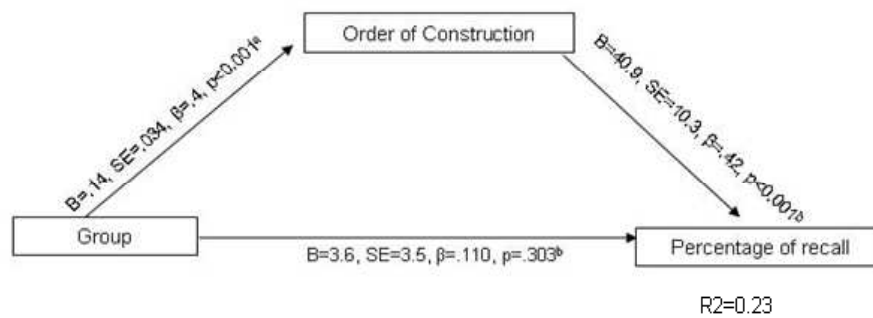
**Figure 4.1 Direct model: Group effect (AN vs HC categories) on percentage of recall**

Mediation Hypothesis 1: *The effect of organisation strategies on group differences in percentage of recall.* As expected, organisational strategies scores had a direct effect on percentage of recall ( $B = 3.8, SE = 1.02, st.\beta = .38, t = 3.8, p < .001, R^2 = .15$ ). In the multiple regression analysis, organisational strategies maintained its effect on the percentage of recall ( $B = 3.28, SE = 1.06, st.\beta = .33, t = 3.08, p = .003$ ) whereas the effect of Group lost its effect falling to non-significant levels ( $B = -5.7, SE = 3.5, st.\beta = -.17, t = -1.6, p = .10$ ). This mediation model

explained twice the amount of the variance in percentage of recall than the direct model Group  $\rightarrow$  Percentage of recall ( $F_{(2,81)} = 8.57, p < .001, R^2 = .18$ ). The Sobel test showed that this mediating effect was significant ( $t = -2.16, p = .03$ ). There were no interactions between Group effect and the effect of Organisational strategies, that is, no moderator effects were found ( $F_{(5,84)} = 0.79, p = .56$ ).

Mediation Hypothesis 2: *The effect of coherence on group differences in percentage of recall.* All the central coherence indices (order, style and coherence index) were included in different mediation analysis provided that the basic assumptions for mediation analysis were maintained: linearity, normality, homogeneity of error variance and independence of errors (Kenny et al., 1998). The coherence index (derived from order and style indices) also had a direct effect on recall ( $B = 18, SE = 4.74, st.\beta = .39, t = 3.8, p < .001, R^2 = .15$ ). In the multiple regression analysis, the coherence index maintained its effect on the percentage of recall ( $B = 15.24, SE = 5.24, st.\beta = .33, t = 2.9, p = .005$ ) whereas the effect of group fell to non-significant levels ( $B = 4.5, SE = 3.7, st.\beta = .14, t = 1.2, p = .20$ ). This model also explained a bigger amount of the variance of percentage of recall than the direct model ( $F_{(2,81)} = 8.0, p < .001, R^2 = .17$ ). The Sobel test showed that this mediating effect was significant ( $t = 2.86, p = .004$ ) and no moderator effects were found ( $F_{(1,80)} = 0.98, p = .30$ ).

Further explorations revealed that the *order index* was the most powerful mediator explaining 23% of the variance (see Figure 4.2). The Sobel test showed that the mediating effect of *order* in the copy trial was highly significant ( $t = 3.05, p = .002$ ). Again, no moderator effects were found ( $F_{(1,80)} = .26, p = .6$ ). Finally, the role of *style index* in a mediating model did not reach significance ( $p = .15$ ) and did not have a moderator effect ( $F_{(1,80)} = 1.8, p = .20$ ).



**Figure 4.2 Order of construction mediates the effect of Group on Percentage of recall**

#### 4.6.3 The effects of demographic and clinical variables on neuropsychological performance

To explore the relationship between neuropsychological, demographic and clinical variables, correlation coefficients were used. Due to the large number of variables obtained from the neuropsychological tasks, the neuropsychological variables entered in the correlation analyses were those measuring main aspects of coherence: time, errors and false claims in the Embedded Figure test, benefit from segmentation in the Block Design test (Un/seg BD), coherence indices in the Rey-Osterrieth Complex Figure test (RCFT), initial pronunciation scores in the Homograph Reading Task (HRT) and total score in the Sentences Completion Task (SCT). Additionally, accuracy in the RCFT was included due to its wide use in the relevant literature.

In the two verbal tasks, the SCT and HRT, a restricted range of cases was found in both AN and HC groups indicating the presence of ceiling effect on the SCT (range = 8 in both groups) and floor effect on the HRT (a range of 4 in HC and 6 in AN). In order to provide an accurate and more reliable indicator of the strength of the relationships between these two neuropsychological variables and the other variables presented here, the verbal variables were transformed into binary dummy-coded variables (in HRT, 0 = no errors in initial pronunciation, 1= errors in initial pronunciation; in SCT, 0 = no local completions and no long hesitation, 1 = either

local completions or long hesitations) and point-biserial Pearson's correlations were used.

Only significant correlations are described below.

#### ***4.6.3.1 Demographic variables***

The relationship between neuropsychological features and variables of age, years of education and estimated intellectual ability measured by NART were explored. In the AN group, age significantly correlated with all the variables of the EFT: median time ( $r_s = .40, p = .008$ ), errors ( $r_s = .39, p = .01$ ) and number of false claims ( $r_s = .32, p = .04$ ). Thus, older participants were less accurate and took longer to find the hidden figures. Intellectual ability was associated with a reduced benefit from segmentation in the BD ( $r_s = .40, p = .01$ ) and with a better performance in the initial pronunciation of homograph in the HRT ( $r = .39, p = .002$ ). Finally, longer period of education was again linked to benefit from segmentation in the BD ( $r_s = .36, p = .02$ ).

In the HC group, the estimated intellectual ability was inversely correlated to the number of errors in the EFT ( $r_s = .42, p = .03$ ) so as was years of education ( $r_s = .39, p < .04$ ). Similarly, in the AN group, initial pronunciation scores in the HRT related to intellectual ability ( $r_s = -.39, p < .02$ ). No age effects on neuropsychological results were found in the HC group (all  $p > .91$ ).

Only the variable 'years of education', on which groups differed, was initially tested as a possible covariate for group differences in the number of errors in the EFT but the assumptions of homogeneity of regression slopes and equality of variance were violated.

#### ***4.6.3.2 Levels of co-morbid symptoms and use of medicines***

##### *Levels of co-morbidity*

Overall, only moderate relationships were found between levels of anxiety, depression and obsessive-compulsive symptoms and a few of the relevant neuropsychological outcomes.

In the AN group, obsessive-compulsive symptoms as measured by scores on the OCI-R related to errors in the pronunciation of the homographs in the HRT, i.e.

the higher the OCI-R scores the poorer the accuracy in the HRT ( $r = .50, p = .001$ ) and correlated negatively with both of the recall parameters of the RCFT: percentage of recall ( $r_s = -.42, p = .03$ ) and accuracy ( $r_s = -.41, p = .04$ ). Also, scores on some sub-scales of the OCI-R were associated with coherence indices in the same task: higher scores on the checking and hoarding sub-scales were moderately related to lower scores in style and coherence indices (all  $r_s$  between .33 to .41, all  $p < .05$ ). Anxiety levels correlated with poorer performance on the HRT ( $r = .37, p = .02$ ).

In the HC group, levels of depressive and anxiety symptoms positively correlated with inaccuracy on the homograph pronunciation in the HRT ( $r = .32$  and  $.40$  respectively, all  $p < .05$ ). The obsessing sub-scale of OCI-R was found to be associated with local processing in the SCT ( $r = .34, p < .03$ ).

Levels of obsessive-compulsive symptoms were examined as a potential confounder variable in the difference between groups on percentage of recall and accuracy in the copy trial of the RCFT, however the main assumptions for ANCOVAs were breached: normality in the case of OCI-R scores distribution and homogeneity of slopes (Group x OCI-R score interaction,  $p < .005$  in both models). Additionally, there was a weak relationship between both dependent variables (i.e. percentage of recall and copy accuracy) and the potential covariate ( $R^2$  below 0.10). Therefore, an ANCOVA could not be carried out.

#### *Effect of use of psychotropic medicines*

The AN group was split according to the regular use of psychotropic medicines at the time of the assessment. As mentioned before, 17 AN patients were on medication and 25 were off medication. No differences in performance were found between medicated and non-medicated patients on any neuropsychological variable performance (all  $p > .09$ ).

#### **4.6.3.3 Clinical variables**

Only a few significant relationships were found between clinical variables such as duration of illness, age of onset, time spent admitted to a hospital, BMI, and neuropsychological variables.

Women with a longer history of illness spent more time finding the embedded figures in the EFT ( $r_s = .38, p = .02$ ).



In the AN group, a relationship was found between the level of starvation measured by BMI and errors in the initial pronunciation in the HRT ( $r = -.31$ ,  $p = .04$ ). In other words, the lower the BMI the higher the accuracy in reading the homographs in context. In the HC group, style index of the RCFT was found to be negatively associated with BMI ( $r = -.33$ ,  $p = .03$ ).

Interestingly, no other significant correlations were found between BMI and all the other neuropsychological variables in either the AN or HC groups.

#### *A comparison between those with binge-purge and restricting anorexia nervosa*

In order to investigate whether different symptoms constellations are associated to different levels of cognitive coherence, the group of women with AN was divided according to the sub-diagnostic categories: binge-purge AN ( $n=13$ ) and restricting AN ( $n= 29$ ) and compared in neuropsychological performance. As the sample sizes were unequal, *Cohen's d* effect sizes were calculated to highlight any possible obscured difference between sub-groups.

Univariate analysis revealed a significant difference between subgroups only in copy accuracy on the RCFT ( $t = 2,64$ ,  $df = 40$ ,  $p = .01$ ,  $d = .91$ ) whereby those with binge-purge sub-type of AN obtained lower scores ( $M = 29.2$ ,  $SD = 2.7$ ) than the restricting type of AN group ( $M = 31.7$ ,  $SD = 2.9$ ). No significant differences were found in any coherence outcome variable. However, an examination of effect sizes revealed medium effects on coherence indices (order, style and coherence indices with  $d$  of .49, .41 and .41, respectively) and accuracy in copy of RCFT ( $d = .40$ ). These medium effect sizes suggest that differences between sub-groups in the aforementioned variables might be hidden by a lack of statistical power due to the small sample size in the binge-purge AN group. Overall, the results would indicate that those with binge-purge type of AN would be less accurate and use more integrative strategies than their comparison restricting AN group on the RCFT.

All other effect sizes were small or negligible varying from  $d .02$  to  $.29$ .

*A comparison between binge-purge anorexia, restricting anorexia and healthy controls*

Taking into account the potential discrepancy in the cognitive profile amongst sub-types of AN, the two sub-groups were then included in a multivariate comparison with the HC group. Kruskal-Wallis tests were carried out due to the lack of normality in the data distribution.

In terms of coherence outcomes, significant differences were found across groups on central coherence indices of the RCFT, number of false claims of the EFT and total local score of the SCT. However only trends were found in the time spent on the EFT differing from the results from the whole group comparison reported above. Table 4.5 displays the results from these analyses on main outcomes of cognitive coherence.

With regards to non-coherence variables, groups differed in copy accuracy (Kruskal-Wallis Test,  $\chi^2 = 6.1, p = .047$ ) and recall ( $\chi^2 = 6.9, p = .03$ ), percentage of recall ( $\chi^2 = 7.0, p = .03$ ), and organisational strategies ( $\chi^2 = 9.8, p = .008$ ). Post-hoc comparisons between groups revealed that in copy accuracy only a statistical trend was found between the HC group and the BPAN group (Mann-Whitney  $U = 179.0, p = .06$ ) and no difference was found between the HC and the RAN group. Also, significant differences were found in recall accuracy between BPAN and HC (Mann-Whitney  $U = 144.0, p = .01$ ) and only a trend between HC and RAN (Mann-Whitney  $U = 543.0, p = .09$ ; HC > RAN > BPAN). However in percentage of recall both affected groups significantly differed from the HC group (Mann-Whitney  $U = 155.0, p = .02$  for BPAN comparison and Mann-Whitney  $U = 436.0, p = .04$  for RAN comparison; HC > BPAN > RAN). Finally, organisation strategies were found to be poorer in the RAN group (Mann-Whitney  $U = 352.5, p = .002$ ) but not in the BPAN group ( $p > .10$ ).

**Table 4.5 A comparison between sub-types of anorexia nervosa and healthy controls on neuropsychological indices of coherence**

	<b>RAN</b> <i>n</i> = 29	<b>BPAN</b> <i>n</i> = 13	<b>HC</b> <i>n</i> = 42	$\chi^2$ <sup>a</sup> df=2	<i>p</i> -value	<b>Group effects<sup>b</sup></b>
EFT medians	8.3 (6.2-2.3)	10.1 (6-4.4)	12.2 (7.9-15.3)	5.2	.08	HC>RAN <i>p</i> =.02
EFT errors	0 (0-1)	0 (0-1)	1 (0-2)	12.2	.002	HC>RAN <i>p</i> =.001 <sup>c</sup> HC>BPAN <i>p</i> =.04
EFT false claims	1 (0-2)	0 (0-1)	2 (0-3)	7.9	.02	HC>RAN <i>p</i> =.07 HC>BPAN <i>p</i> =.01 <sup>d</sup>
BD benefit from segmentation	39% (28-64)	35% (27-50)	39 % (28-50)	1.2	.54	
RCFT order	2 (1.5-2.3)	2.3 (1.9-2.7)	2.5 (2.2-3)	14.5	.001	HC>RAN <i>p</i> <.001 <sup>c</sup>
style	1.5 (1-1.7)	1.7 (1-1.8)	1.7 (1.5-1.8)	13.1	.001	HC>RAN <i>p</i> <.001 <sup>c</sup>
coherence	1.3 (.95-.15)	1.5 (1.2-1.8)	1.6 (1.5-1.8)	17.8	<.001	HC>RAN <i>p</i> <.001 <sup>c</sup>
SCT local processing	1 (0-2)	1 (0-2.5)	0 (0-1)	8.2	.02	HC>RAN <i>p</i> =.04 HC>BPAN <i>p</i> =.02
HRT initial pronunciation	15 (14-16)	15 (14.5-16)	15 (14-16)	.05	.98	

RAN: restricting anorexia nervosa; BPAN: binge-purge anorexia nervosa; HC: healthy controls

<sup>a</sup> = Data does not fit the assumptions of parametric testing therefore Kruskal-Wallis Test was used. Median values and interquartile ranges displayed (Q25-Q75).

<sup>b</sup> = Mann-Whitney U Test

<sup>c</sup> = Results that remained significant (*p*<0.05) after Hochberg correction for multiple testing (Hochberg, 1988). <sup>d</sup> = Results dropped to trend levels (*p*=.08).

Overall, the results explained above show that the RAN group display a profile much more like that obtained from the whole group of women affected with AN. It is worthy to note that the RAN group was overrepresented in the whole group in comparison with the small sample in the BPAN group.

The BPAN group differed somewhat from the RAN and the whole AN group in that they were more like the HC group in using global processing strategies in the visual-spatial tasks (e.g. higher coherence indices, better organisational strategies, and no advantage in local processing in the EFT) but preserved accuracy in the EFT

(e.g. less errors and false claims). Interestingly, the BPAN group showed less accuracy in the copy trial of the RCFT which differs from both the RAN and HC groups.

## 4.7 Discussion

The objective of this first case-control study was to examine the concept of central coherence in women currently suffering from anorexia nervosa (AN). Overall, the findings reported here support the general hypothesis that people with AN have *weak central coherence* with strengths in detail-focused processing and a relative weakness in global integrative processing, particularly in the visual-spatial domain. This profile is similar to the cognitive processing style shown by people with high functioning autism (Happé and Frith, 2006) and Aspergers (Jolliffe and Baron-Cohen, 1997).

### 4.7.1 Discussion of predictions

Most of the specific predictions described in the hypothesis section were confirmed however a few of them failed to be endorsed by the data or were rejected.

Specifically, the results supported the predicted superiority of the AN group in performance on the Embedded Figure Test (EFT) in both speed and accuracy. This observation provides evidence to favour the superior local processing predicted for the AN group relative to the matched healthy control group (HC) and corroborates the findings of Tokley and Kemps (Tokley and Kemps, 2007). As described in the systematic review (see chapter 3) it must be noted that previous literature contradicts these more recent studies using the EFT in AN (Basseches and Karp, 1984, McLaughlin *et al.*, 1985, Sours, 1969). Methodological differences such as whether or not memory is a component of the task may explain the variation.

On the other hand, the performance of the AN group in the Block Design Test (BD), which is thought to benefit from a strong local processing, produced conflicting results. The AN group was comparable to the HC group in the coherence indicator of the tasks (percentage of benefit from pre-segmentation of designs) and was slower in completing the segmented sub-test of the BD. In the systematic review the case of BD was discussed and part of that discussion fits well with these

outcomes. Although BD has been proposed as one of the ‘premier’ tests to measure superiority in detail processing in autism (Happé and Frith, 2006, Shah and Frith, 1993) the nature of the task is complex and the interpretation is unclear. It has been argued that a good balance between both the analytical and integrative cognitive processes accounts for a successful outcome on the BD (Spreen and Strauss, 1998, Strauss *et al.*, 2006). Therefore the conflicting results found in the present study may be explained by a potential imbalance between global and local visual-spatial processing displayed by the group with AN. Also, observations of the performance of people with AN on this task revealed frequent delays in finishing the designs due to perfectionist tendencies (e.g. making an effort to ensure that blocks perfectly fitted to each other) and violations of configuration in preserving the details (e.g. exaggerating the size of a detail of a design without taking into account the design as a whole). The latter has been described as a possible type of failure that those with weak coherence might produce (Happé and Frith, 2006).

The predictions related to weaknesses in global integration processing were in the main part supported by the results of this study. It was found that the AN group displayed a more fragmented drawing style in the Rey-Osterrieth Figure Test expressed in significantly lower coherence indices than the HC group. Similarly, relative difficulties in global processing were found in the verbal domain, particularly in the local score of the Sentence Completion Task (SCT). Nevertheless, there were no signs of an extreme bias towards detail in verbal processing as local completions were as rare as in the HC group and no differences were found in reading the homographs in context (HRT).

The functioning displayed by the AN group in the SCT task resembles the type of performance of parents of people with autistic spectrum disorders (ASD) who are more likely to have a normal intellectual ability than their probands. People with ASD make more errors on context-appropriate pronunciation when reading the homographs (Happé, 1997, Jolliffe and Baron-Cohen, 1999) and people with high functioning ASD have been found to produce more local completions than matched healthy controls in the SCT (Booth, 2006). Parents, especially fathers, of people with ASD, like the AN group here, hesitated longer in finding an appropriate ending to the sentences but would not often make local completions (Happé *et al.*, 2001). These data support the prediction referred to in the secondary hypothesis that proposed less impaired global processing in the verbal domain in comparison with the visual-

spatial. The relationship found between performance in the HRT and intellectual abilities might have accounted for the good performance of both the AN and HC group on this task.

As expected, the sub-categories within the AN group (restricting anorexia nervosa: RAN, and binge-purge anorexia nervosa: BPAN) overall displayed a similar cognitive profile. However, some differences were observed, particularly in the decreased accuracy of the BPAN sub-group (lower accuracy scores in the copy trial of the RCFT, more false claims and errors in the EFT). These results might be seen as potential signs of cognitive impulsivity but the lack of difference with the HC group, except for the performance in the RCFT accuracy, prevents such a conclusion. Other possible explanations might be careless drawing or lack of interest in the task. Finally, although there were no differences between the BPAN and RAN groups in terms of coherence indices of the RCFT, the former appeared not to be impaired in the between group comparison with the HC group. These results however need to be considered tentative as the lower power provided by sub-dividing the AN group might have obscured potential difference between groups as suggested by the inspection of the effect sizes.

The subsidiary hypotheses (not directly related to central coherence outcomes) were endorsed by the outcomes of this study. Thus, women with AN showed poorer recall in the RCFT and the percentage of recall was mediated by the coherence indices, especially by order of construction which explained around a quarter of the percentage of recall variance.

The poor recall in the RCFT has commonly been reported in previous studies in AN (Mathias and Kent, 1998, Pendleton Jones *et al.*, 1991, Sherman *et al.*, 2006). A possible explanation for part of the low level of recall shown by people with AN might be explained by the possible effect that the drawing style displayed during the copy trial has on non-verbal memory (Strauss *et al.*, 2006). Sherman and colleagues (2006) examined the process as well as the outcome of this task. Their study was replicated in this work and their results corroborated. Their process measure is conceptualised as organisational strategies attributed to the executive functioning (for details review Savage *et al.*, 1999) rather than central coherence. Poor organisational strategies might relate to impaired executive functions (specifically those of planning and organisation), whereas weak coherence refers to a default detailed-focus *cognitive style* (or *local bias*) not totally explained by executive dysfunctions (see

Happé and Frith, 2006). The mediation analyses carried out in this study to explain group differences in percentage of recall were consistent both with the organisational strategy account of Sherman *et al.* (2006) as well as the central coherence account.

#### 4.7.2 Possible confounders

Levels of co-morbidity did not have an important effect on neuropsychological performance in this study. Only moderate or small correlations were found between levels of co-morbid symptoms, mainly obsessive-compulsive symptoms, and some aspects of the neuropsychological performance. Importantly, obsessive-compulsive traits have an impact on the prognosis of AN and may be both moderating and mediating factors in treatment (Crane *et al.*, 2007).

The few significant correlations between obsessive-compulsive symptoms, anxiety, and depression and coherence outcomes (most of which lost significance after correction for multiple testing) are in line with what has been reported in the literature with regards to a more narrow cognitive processing linked to a obsessive-compulsive symptoms (Bohne *et al.*, 2005, Mataix-Cols *et al.*, 2003, Savage *et al.*, 1999), and a bias towards detail in low mood syndromes (anxiety and depression) (Happé and Frith, 2006).

BMI was weakly and negatively correlated with the error score in the HRT but there were no correlations between the degree of starvation and performance in the other tasks, suggesting that weak central coherence might be a trait independent of BMI. This possibility will be addressed in the following two chapters of this thesis which describe the investigation of coherence in groups with normal BMI (bulimia nervosa and recovered samples). This exploration is guided by the conceptualisation of weak coherence as a potential endophenotype for eating disorders.

#### 4.7.3 Limitations of the study

This study has certain limitations.

Firstly, the cross-sectional design of the study makes it difficult to rule out the effect of starvation on the weak coherence reported to be characteristic of this AN sample. However, only one aspect of the neuropsychological examination was found to be related to BMI. All other indices were unrelated which might suggest that weak coherence would be independent of the underweight state characteristic of AN.

Secondly, after splitting the AN group into its two main diagnostic sub-categories (restricting versus binge-purge anorexia nervosa) unequal sample sizes were obtained. Moreover, the group with a RAN type of disorders was overrepresented in this study (69%) in comparison with those with a BPAN type of anorexia (31%). The resulting reduced lack of statistical power might have precluded the identification of significant differences between the sub-groups. An examination of effect sizes, which are independent of sample size effects, uncovered potential differences, for example, in the coherence indices of the RCFT. As the coherence indices of the RCFT are core indices of general coherence in this study, a future study with larger and equal sample sizes would be needed to clarify whether those with BPAN have weak visual coherence as shown by those with RAN.

Thirdly, unfortunately, the verbal coherence tasks used in this study were somewhat insensitive to variation in this high IQ, well educated population (the majority of both AN and HC populations scored at the extreme end of the scale with little deviation) and ceiling/floor effects were observed. There is a need to look for more sensitive verbal tasks. A suitable alternative task might be the California Verbal Learning Test which Savage and collaborators have used to investigate verbal organisational strategies in obsessive-compulsive populations with interesting results (Savage *et al.*, 2001, Savage *et al.*, 2000). In future studies it would be interesting to have a test battery which taps into these different dimensions and which has been field tested in a group with an equivalent mean intellectual ability to the AN group.

In fourth place, the missing data of the intellectual ability from the first 20 participants may account as a limitation in terms of the samples matching. However, results in this study indicated only a weak association between intellectual ability and neuropsychological performance. Furthermore evidence from literature in AN have shown general equivalence between AN population and norms in terms of intellectual ability (Southgate *et al.*, 2006).

Finally, this clinical sample had a severe, chronic AN and the results may not generalize to other ED populations (e.g. less severe AN or bulimia nervosa). Studies reported in Chapters 5 and 6 will help to clarify aspects of these questions.



#### 4.7.4 Strengths of the study

There are a number of strengths associated with this study. Firstly, this is the first study to our knowledge that directly addresses the concept of coherence in people with AN. Other studies have utilized the concept of coherence to explain the results found in neuropsychological tasks but were not intended to primarily examine this concept (Gillberg *et al.*, 2007, Southgate *et al.*, 2007).

Secondly, this study included a large sample of clinical and control participants who were matched for gender, age and intellectual ability thereby fulfilling the requirements of sample size calculation. Unfortunately, as already mentioned, the sample size in the AN was insufficient for sub-grouping examination.

Thirdly, the recruitment strategy used for this study allowed the attainment of participants from varied sources overcoming the treatment seeking bias that is often typical of recruitment (Southgate *et al.*, 2006) and increasing the possibility of the samples to include people with various degrees of illness severity. In spite of this effort, the AN group was in the main part a severe group with a long history of illness and perhaps more motivated to help with research.

Finally, an additional endeavour of the study was to explore relationships between variables that could act as confounders on the neuropsychological outcomes between groups, especially in terms of co-morbid symptom levels and use of medicines, and to control them through the use of statistical techniques.

#### 4.7.5 Clinical and research relevance of the findings

Clinical observations of patients with AN converge with the idea of an extreme attention to detail in patients with AN (Anderluh *et al.*, 2003, Kemps *et al.*, 2007, Tokley and Kemps, 2007). Some of the behaviours exhibited typically by someone suffering from AN could be described as being under the umbrella of weak coherence. Examples of such behaviours are: the focus on calorie counting instead of their nutritional health, the attentional bias towards specific body parts (Dobson and Dozoi, 2004), difficulties in attending to the long-term consequences of some of the dangerous behaviours in which they engage, focus in details in other aspects of life beyond eating and weight/shape concerns, and the core characteristic of body image distortion (Gillberg *et al.*, 1996, Sherman *et al.*, 2006). Characteristics such as the aforementioned plus other irregularities of the information processing such as

cognitive inflexibility found in AN (e.g. Steinglass *et al.*, 2006, Tchanturia *et al.*, 2004a) may act as maintaining factors, as suggested by Schmidt and Treasure (Schmidt and Treasure, 2006). Treasure (Treasure, 2007) argues that new treatments for AN should be tailored to specifically address predisposing or maintaining factors of the illness such as these anomalies in information processing. It is possible that specific treatment modules to correct informational processing bias may improve the outcome of AN by targeting the compulsive and over-analytical traits of the illness. Tchanturia and collaborators have developed a module of cognitive remediation therapy (CRT) specifically designed for people with AN (Davies and Tchanturia, 2005, Tchanturia *et al.*, 2007a, Tchanturia *et al.*, 2006a). This intervention has been recently piloted in inpatient settings, addressing both set-shifting difficulties and weak central coherence with promising results (Tchanturia *et al.*, submitted). A similar but less intensive module has also been developed for outpatient settings. These modules of treatment can be included as part of the standard treatment for patients with AN. Details of these interventions will be provided in Chapters 8 and 9.

As part of these specific modules of interventions, the neuropsychological assessment of coherence within routine assessment in clinical settings might be of use in selecting appropriate interventions for a particular patient e.g. specific training to improve global strategies. The information resulting from these assessment would also be a useful tool in sharing information with carers in family assessments to help them to better understand the behaviour of their relative with ED and reduce criticism (Treasure *et al.*, 2008). Finally, clinicians may integrate their understanding of cognitive styles in people with AN into their clinical practice and help to promote and reinforcing therapeutic interventions and behaviours that enhance global processing and reduce the bias towards detail.

In terms of research, there are some specific and broader potential contributions to emerge from this work.

Specifically, the mediational role of weak coherence in the RCFT has both research and clinical implications. For example, it could help to explain inconsistent results from memory tasks in AN (Southgate *et al.*, 2005b) and perhaps some of the compulsive checking behaviours in AN. Indeed, in this study checking symptoms were related to the coherence index of style in the AN group. Savage and collaborators noted that their findings in AN, without co-morbid OCD, replicated those they had obtained in people with obsessive-compulsive spectrum disorders

(Deckersbach *et al.*, 2000, Savage *et al.*, 1999, Savage *et al.*, 2000). Interestingly, a recent working party set up to consider diagnostic issues for the DSM V relating to OCD have proposed that both ED and autistic spectrum disorders (ASD) could be encompassed within a broad obsessive compulsive spectrum umbrella (Hollander *et al.*, 2007). In relation to this, it is noteworthy that we found that OCI-R scores were related to recall accuracy in the RCFT and that subscales of the same test were associated with other indices of weak global processing.

Broadly speaking, the findings reported here may contribute to a better understanding of the similarities and differences between the cognitive phenotype of those with ASD and those with AN. Whereas in ASD the evidence is clear to support the superior local processing aspect of weak coherence, the evidence is less conclusive with regards to difficulties in global processing (Happé and Booth, 2008, Happé and Frith, 2006). The data obtained from this study in AN would claim the opposite: the current evidence is more consistent in favour of the weak global processing aspect of weak coherence (particularly in those with restricting type of AN), but less conclusive with regards to the superiority in local processing.

#### **4.8 Conclusion**

To conclude, this study examined the cognitive style of weak coherence in women with a current diagnosis of anorexia nervosa relative to a healthy control group.

The results from this piece of research suggest that women with AN have *weak central coherence* with a bias towards local rather than global processing, particularly in the visual-spatial domain. It seems, according to the current evidence, that diagnostic sub-categories (RAN versus BPAN) would display some differential features mainly in that BPAN group would be less impaired in visual-spatial global processing and would be less accurate across tasks. Finally, the observations produced by this study enrich our comprehension of the cognitive functioning of people with AN and set the scene for the further exploration of the hypothesis of weak coherence across diagnostic categories as an endophenotype for ED.

## 5 WEAK CENTRAL COHERENCE ACROSS DIAGNOSIS: IS THIS COGNITIVE STYLE RELEVANT FOR BULIMIA NERVOSA? <sup>7</sup>

### 5.1 Introduction

This chapter describes the second experimental study of this thesis which was aimed at examining the concept of central coherence in women with bulimia nervosa (BN) and addressing similarities and differences with those with anorexia nervosa (AN). This study employed the same procedures and measures used in the investigation of central coherence in AN, as previously outlined in Chapter 4, and endeavoured to further the examination of weak coherence as a potential endophenotype for eating disorders (ED).

### 5.2 Background and development of the study

As mentioned in Chapter 1, the examination of putative cognitive endophenotypes in ED has been mainly limited to weaknesses in set-shifting ability which would fit most of the criteria required of an endophenotype for AN (i.e. present in the acute phase of the illness, after recovery and identified in higher rates in unaffected relatives than in the normal population), although there is less evidence available for BN (Bulik *et al.*, 2007b, Roberts *et al.*, 2007, Tchanturia *et al.*, 2004a).

As the currently available evidence shows, the cognitive functioning of people suffering from BN has been generally less intensively investigated than in AN (Duchesne *et al.*, 2004, Southgate *et al.*, 2005b). It might be possible that some of the few problems reported in the cognitive functioning of BN play a role as underlying markers of risks in BN (Steiger and Bruce, 2007) but the scarcity of systematic examination of these characteristics in this group prevent the formulation of stronger conclusions (Southgate *et al.*, 2006). Therefore further cognitive exploration in this group is needed.

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<sup>7</sup> An version of this chapter has been published: **Lopez, C., Tchanturia, K., Stahl, D. & Treasure, J.** (2008c). Central coherence in women with bulimia nervosa. *International Journal of Eating Disorders* **41**, 340-347.

Differences and similarities between cognitive processing observed in BN and in the acute phase of AN have been noted. Main differences are related to ‘cognitive impulsivity’ which would be characteristic of people with BN or bulimic type syndromes as opposed to AN (Kaye *et al.*, 1995, Steiger and Bruce, 2007, Toner *et al.*, 1987) and may mirror impulsive traits seen at the phenotypic level in least about one-third of individuals with BN (Engel *et al.*, 2005, Steiger and Bruce, 2007, Wonderlich *et al.*, 2005). However, this characteristic trait in BN has been recently contradicted by a study in which no differences between AN and BN in cognitive impulsivity were found (Southgate *et al.*, 2007).

A possible explanation for these conflicting results might be found in the different methods and procedures employed in previous studies and more importantly, in the diversity of participant samples (Southgate *et al.*, 2007). For example, in a different a study it was demonstrated that the subgroup of laxative abusers were more impulsive than those without laxative abuse and healthy controls (Bruce *et al.*, 2003). Moreover, there is an increasing consensus in support of the intradiagnostic heterogeneity in the spectrum of bulimic disorders (Eddy *et al.*, 2008, Steiger and Bruce, 2007). Steiger and Bruce (2007) have argued that there are at least three clear distinct bulimic subtypes such as a ‘psychologically intact’ group although with perfectionistic tendencies; an ‘overregulated’ or ‘compulsive’ group; and a ‘dysregulated’ or ‘impulsive’ group. It might be possible that these groups show different patterns of neuropsychological performance with more or less impairment.

The similarities found in the cognitive functioning between people with BN and AN in some studies, on the other hand, may also reflect this variability in the bulimic subtypes. Some of these similar cognitive characteristics that have been mentioned in the literature are reduced vigilance (Laessle *et al.*, 1990, Laessle *et al.*, 1989), poor attention (Pendleton Jones *et al.*, 1991, Rosval *et al.*, 2006), and the aforementioned poorer set-shifting abilities (Roberts *et al.*, 2007, Tchanturia *et al.*, 2004a). These shared characteristics lie at the heart of the transdiagnostic approach (Fairburn *et al.*, 2003, Wade *et al.*, 2006).

As demonstrated in Chapter 4, *weak central coherence* in the visual-spatial and verbal domain was found to be a characteristic of most people with acute AN, particularly in women suffering from restricting AN. This cognitive style seems to be associated with some obsessive-compulsive characteristics, one of the well

documented predisposing factors for an ED (Anderluh *et al.*, 2003, Jacobi *et al.*, 2004).

As illustrated in the systematic review of the literature of information processing styles in ED patients (see Chapter 2) only a few studies have explored the concepts of global and local process in BN and none has directly targeted central coherence. The tentative conclusions from the review are that people with BN display less difficulty in tasks where a global rather than a local processing strategy is adaptive than do people with AN (Murphy *et al.*, 2002, Pendleton Jones *et al.*, 1991) but still perform poorer than healthy controls (HC). In addition people with BN seem to be better than people with AN at detailed focused processing but not better than healthy comparison groups. These findings warranted further and more specific examination.

### **5.3 Aims**

The aim of this study was threefold (1) to add to our understanding of the cognitive functioning of people with BN through the examination of the concept of central coherence in women with this illness in comparison to a healthy control group, (2) to reveal whether the concept of weak central coherence is relevant for BN as shown for AN, and (3) to examine similarities and differences between the profile of women with BN and AN in cognitive coherence at both verbal and visual-spatial processing domains.

### **5.4 Methods**

#### **5.4.1 Study Design:**

This study employed a cross-sectional study design.

#### 5.4.2 Participants:

Forty-two women meeting the DSM-IV diagnostic criteria for BN and 42 healthy controls (HC) matched for sex, age and intellectual ability took part in this study. The HC group is the same sample that participated in the previous cross-sectional study comparing women with AN and HC (see Chapter 4).

##### ***5.4.2.1 Participants with current diagnosis of Bulimia Nervosa***

The largest number of BN participants was recruited from the general community ( $n = 19$ , 45.2%) via advertisements of the study (Ethic reference number 20/05) including through the media (e.g. TV programs and news papers advertisements of the general research activity of the Eating Disorders Research Unit). The other half of participants were ascertained from the EDU volunteer database ( $n = 7$ , 16.7%), clinical cases of the eating disorders unit based at the South London & Maudsley NHS Trust (including Maudsley & Guy's Hospitals Outpatient clinics ( $n = 7$ , 16.7%), the student population of the Institute of Psychiatry and King's College London ( $n = 8$ , 19.0%), and the staff population of King's College London ( $n = 1$ , 2.4%). Please see Chapter 3 for full details of recruitment strategies.

Diagnosis of BN was made following the DSM-IV criteria based on the *EATATE* interview (Anderluh *et al.*, 2003). Five women in the BN group (12%) met the criteria for non-purging BN and 37 (88.9%) for purging BN. Eighteen women with BN (42.9%) had a prior history of AN (fulfilling criteria for AN according to the DSM-IV for more than 3 consecutive months). Seven women with BN (16.7%) were taking psychoactive medication (four of them were on SSRI antidepressants). None of them were undergoing inpatient treatment.

##### ***5.4.2.2 Healthy control participants***

The healthy control group (HC), consisting of 42 women, was the same sample as the one described in Chapter 4.

#### 5.4.3 Measures:

This study replicated the investigation of central coherence in AN using the same measures as the ones already described in Chapters 4.

The battery of measures consisted of the EATATE semi-structured interview utilised for diagnosis purposes (Anderluh *et al.*, 2003), the modified version of the EDE-Q used as screening for HC (Fairburn and Beglin, 1994), a series of self-report questionnaires assessing levels of comorbid symptoms of obsessive-compulsive disorders (Foa *et al.*, 2002), depression and anxiety (Zigmond and Snaith, 1983) and the central coherence battery. This included: The Embedded Figure Test – **EFT** (Witkin *et al.*, 1971); the Un-segmented Block Design Test – **Un/seg BD** (Happé *et al.*, 2001, Shah and Frith, 1993); the copy and recall trial of Rey-Osterrieth Complex Figure – **RCFT** (Osterrieth, 1944); the Sentence Completion Task – **SCT** (Happé *et al.*, 2001); and the Homograph Reading Task – **HRT** (Happé, 1997, Jolliffe and Baron-Cohen, 1999). The National Adult Reading Test – **NART** (Nelson and Willison, 1991) was also administered to the majority of the sample.

#### 5.4.4 Procedure

The same procedures as described in the AN study were used throughout. All participants in the clinical sample (BN) agreed to be weighed on the day of testing. The NART test was not obtained from the first 19 participants (six from the BN group and 13 of the HC group). Three women of the BN group did not return the OCI-R measure and one from the HC group did not return the HADS questionnaire. Their data were nevertheless included in the analyses of the main outcome measures (central coherence battery).

#### 5.4.5 Data analysis

The same data analysis procedures as described in Chapter 3 and 4 were used. For the comparison of more than two groups, Kruskal-Wallis Test for non-normally distributed data was used. To determine which groups differ after Kruskal-Wallis tests, between groups differences were explored with Mann-Whitney U tests and *p* values were corrected with Bonferroni adjustments (new alpha = .05/number of comparisons) in order to reduce the possibility of Type I errors.



## 5.5 Hypotheses and Predictions

Given that people with BN share some similarities on the obsessive-compulsive phenotype with people with AN (von Ranson et al., 1999), high anxiousness, and 50% of their genetic risk (Bulik *et al.*, 2007b), the primary hypothesis was that on a group level women with BN would be similar to those with AN in that they would show weaker global processing and contextual integration, and superior detail processing relative to a healthy control group (HC). However, the cognitive profile of individuals with BN was not expected to be as extreme as that seen in AN. Based on existing cognitive literature (see Chapter 1) and the heterogeneity described in terms of phenotypic constellations (Steiger and Bruce, 2007), it was hypothesised that the cognitive profile of people with BN would be an intermediate between AN and HC associated with a lower degree of impairment seen in BN (Bowers, 1994) and more similar to that seen in those with binge-purge type of AN. Finally, as part of the sample had a past history of AN, it was hypothesised that the cognitive functioning of those with lifetime AN would be weaker in central coherence than in the ‘pure’ bulimia nervosa subgroup (without past AN) i.e. more alike to the current AN group (Eddy et al., 2008).

### 5.5.1 Central coherence predictions on specific neuropsychological performance

According to the central coherence theory, the following predictions with regards to cognitive performance on the central coherence battery of tests were made. Women in the BN group would:

- Be faster than HC in identifying the hidden figures in the Embedded Figure Test (EFT).
- Benefit less from segmentation of the designs in the Block Design Task (Un/seg BD).
- Display a bias towards detailed processing in the Rey-Figure Complex Task (RCFT) relative to the HC (lower central coherence indices).
- Show decreased use of the context in accurately pronouncing the homographs in the Homograph Reading Task (HRT) and would show more difficulties than the HC in finding appropriate answers to the Sentence Completion Task (SCT).

Also, group differences in percentage of recall in the RCFT would be partly explained by drawing style but to a lesser degree than in the model developed for AN.

Finally, women in the BN group would show more signs of cognitive/behavioural impulsivity which will differentiate their performance from the AN group, i.e. they would be faster and make more errors across tasks (less accuracy).

## **5.6 Results**

### **5.6.1 Demographic and Clinical Characteristics**

The results of demographic and clinical characteristics are shown in Table 5.1.

People with BN and HC were comparable in age, years of education, BMI and estimated intellectual ability (all  $p > .05$ ).

The BN group scored higher on self-report measures of anxiety, depression and obsessive-compulsive symptoms (all  $p < .05$ ). The scores in these psychopathology dimensions represent levels of severity and they do not indicate a clinical diagnosis.

According to the EATATE interview, 18 women in the BN group (42.9%) had co-morbid psychiatric diagnoses: 13 fulfilled criteria for major depression, four for OCD, two for alcohol abuse, one for dysthymia, one for panic disorder and one for generalized anxiety disorder. Four women in this group had more than one co-morbid diagnosis.

The severity of BN was operationalised according to previous literature as duration of illness (Keel *et al.*, 1999, Reas *et al.*, 1999) and/or current use of more than one purging method (Edler *et al.*, 2007). The mean duration of illness was 10.8 years ( $SD=8.32$ ) and 12 women (28.6%) used multiple purging methods.

The significant results displayed on Table 5.1 remained significant after Hochberg's improved Bonferroni correction for multiple testing (Hochberg, 1988) at  $p < .05$ .

**Table 5.1 Demographic and clinical characteristics of BN and HC groups**

	n		BN	HC	Test statistic		<i>p</i> -value	Effect size ( <i>d</i> )
	BN	HC			t-test <sup>a</sup>	MW <sup>b</sup>		
Age (years) <sup>a</sup>	42	42	27.0 (7.2)	26.3 (6.4)	.52	n.a.	.61	.10
Number years of education <sup>b</sup>	42	42	17 (14-17)	17 (14.7-19)	n.a.	327.5	.07	.39
Estimated intellectual ability <sup>a</sup>	38	27	111.8 (6.9)	112.2 (5.4)	-.25	n.a.	.81	.06
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	42	42	21.7 (2.4)	21.9 (2.7)	-.69	n.a.	.50	.08
Anxiety HADS <sup>a</sup>	42	41	12.4 (4.2)	6.0 (3.2)	7.8	n.a.	<.001	1.72
Depression HADS <sup>b</sup>	42	41	7.0 (3-12)	2.0 (1-3)	n.a.	248.9	<.001	1.54
OCI-R <sup>b</sup>	39	42	15 (8-31)	6.5 (3-10)	n.a.	398.5	<.001	.95

t-test<sup>a</sup>= test statistics for t-test pairwise comparisons for data normally distributed, *M* and *SD* values are displayed.

MW<sup>b</sup>= test statistics for Mann-Whitney *U* for data not normally distributed, *Mnd* and *Q* values are displayed.

n.a. = not applicable.

### 5.6.2 Neuropsychological function

The results of the neuropsychological tests that would benefit from a local processing bias are shown in Table 5.2. This table also displays the statistical comparison on cognitive performance between BN and AN groups. The AN group, described in full in Chapter 4, was equivalent in age, IQ and years of education to the BN group described here (all *p* > .15).

### **5.6.2.1 *Embedded Figures Test***

Participants with BN were much faster in finding figures hidden in a complex background than the HC group. No differences between groups were found in the number of false claims ( $p = .65$ ) or in the number of time-out errors ( $p = .12$ ).

### **5.6.2.2 *Un-Segmented Block Design Task***

There were no differences between groups in the segmented and un-segmented sub-tests of the BD in terms of times or errors (all  $p > .12$ ). There was a trend for the BN group to benefit slightly less from the pre-segmentation of the designs in comparison with the HC group ( $M = .35$ ,  $SD = .15$  versus  $M = .40$ ,  $SD = .16$ ,  $t = -1.7$ ,  $p = .09$ ).

**Table 5.2 Between groups comparison results in neuropsychological tasks that benefit from a detail focused processing.**

	<b>BN group n = 42</b>	<b>HC group n= 42</b>	<b>Test t-test<sup>a</sup></b>	<b>statistic MW<sup>b</sup></b>	<b>p-value</b>	<b>d</b>	<b>AN group* N=42</b>	<b>p-value *</b>	<b>d *</b>
EFT total time taken (medians)	6.9 (4.4-12.3)	12.2 (7.9-15.3)	na	539.0	.002 <sup>c</sup>	.69	8.6 (6-14)	.14	.33
EFT number timeout failures	0.5 (0-1)	1 (0-2)	na	717.0	.12	.35	0 (0-1)	.001	.82
EFT false claims	2 (1-3)	2 (0-3)	na	831.5	.65	.05	1 (0-1.25)	<.001	.84
Un/segmented Block Design	41.2 (34.3-49.8)	44.8 (36.5-62.7)	na	709.0	.12	.17	52.1 (39.5-76.2)	0.02 <sup>c</sup>	.56
Segmented Block Design	27.8 (24.8-31.2)	27.7 (25.5-31.5)	na	838.0	.69	.04	30.1 (26.6-37)	0.01 <sup>c</sup>	.58
Benefit from Segmentation	35.1 (14.7)	40.9 (16.3)	-1.7	na	.09	.30	41.3 (17.0)	.08	.39

EFT: Embedded Figures Test

\*= AN results (for details see chapter 6) and pairwise comparison results between AN and BN

t-test<sup>a</sup>= t test statistics for t-test pairwise comparisons for data normally distributed, *M* and *SD* are displayed

MW<sup>b</sup>= U test statistics for Mann-Whitney *U* for data not normally distributed, *Mdn* and upper and lower quartiles (*Q* 25-*Q* 75) are displayed.

na = not applicable.

<sup>c</sup> = Results that remained significant (p<0.05) after Hochberg correction for multiple testing (Hochberg, 1988).

In terms of cognitive performance on tasks where global processing strategies are more adaptive, this study revealed some discrepancies in skills patterns according to modalities i.e. visual-spatial modality measured by RCFT versus verbal modality measured by the SCT and HRT as described below. Table 5.3 displays these results along with the comparison between BN and AN groups which will be discussed later in this chapter.

### **5.6.2.3 *Rey-Osterrieth Complex Figure Test***

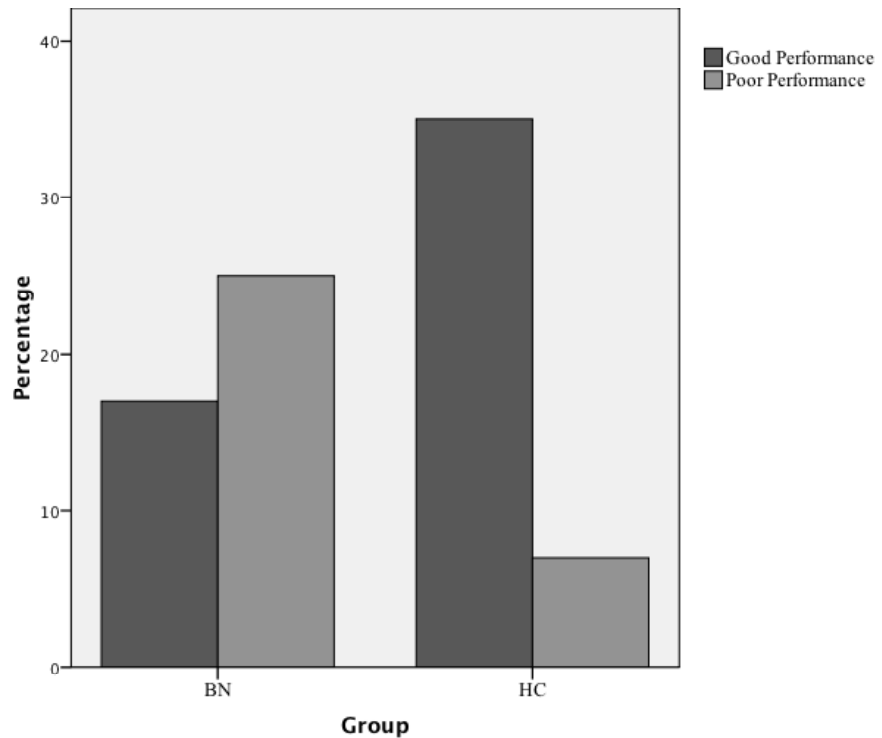
The BN group obtained lower scores in all the central coherence indices with medium effect sizes ranging from  $d = .57$  to  $.66$  (all  $p < .005$ ). These results demonstrate that people with BN displayed a preferential detail focused approach during the copy of the complex figure.

### **5.6.2.4 *Sentence Completion Task***

The BN group showed greater difficulties in global processing than the HC group as measured by the time taken to offer an appropriate answer to the local/global conflicting sentences ( $p < .001$ ). Also, there was a trend in the BN group in making more local completions than the HC group ( $p = .06$ ) although this was a rare event in both groups.

The same procedure as previously used to analyse the results of the AN versus HC study was replicated here. Thus, the proportions of people with ‘good’ and ‘poor’ performance were compared based on the score for local completions and hesitations in this task. As a reminder, ‘poor’ performance was defined as having one or more local completions, and/or two or more long hesitations in the experimental sentences. Those with ‘good’ performance did not make local completions at all and had none or only one long hesitation in the experimental items. A significant difference was found between women with BN and HC in the proportion of participant displaying poor performance in the task.

As shown in Figure 5.1, in the BN group 59.5 % ( $n = 17$ ) had ‘poor’ performance versus only 16.7 % ( $n = 7$ ) in the HC group ( $\chi^2 = 1.63$ ,  $df = 1$ ,  $p < .001$ ).



**Figure 5.1 Good versus Poor performance in the SCT**

#### 5.6.2.5 Homograph Reading Task

None of the participants showed difficulties reading the words in the pre-test list out loud. Women with BN made more errors in the initial pronunciation of the homographs than the HC group. This difference was mainly due to the poor performance in reading the homograph when the context was provided before a rare pronunciation of the homograph (Mann-Whitney  $U = 697.5$ ,  $z = -2.2$ ,  $p = .03$ ). There was no difference in all the other conditions (all  $p > .11$ ). However, the overall differences dropped to non-significant levels after correction for multiple testing. Also, there was no difference in the number of participants making errors across the different conditions of the test ( $\chi^2 = 0.46$ ,  $df = 1$ ,  $p = .50$ ).

Independently of the number of errors in the initial pronunciation, an unexpected significant difference in the proportion of people who made self-corrections was found. Thus, women with BN tended to correct themselves in a higher proportion than the women in the HC group (85.7 % in the BN group versus 16% in the HC group ( $\chi^2 = 2.6$ ,  $df = 1$ ,  $p < .001$ ).

The effect of the context position was explored using Wilcoxon's Signed Rank Tests within in each group. Both groups performed better when the context preceded the pronunciation of the homograph indicating that BN and HC groups were sensitive to the context position. However, this relative advantage of having the context preceding the homographs was statistically significant with respect to the 'rare' pronunciation conditions only (HC:  $z = -2.18$ ,  $p = .029$ ; AN:  $z = -2.27$ ,  $p = .02$ ). There was also a trend in the BN group for an advantage of context in the frequent condition ( $z = -1.82$ ,  $p = .07$ ) but not in the HC group ( $z = -1.21$ ,  $p = .23$ ).

Finally, the effect of the context between groups was examined using difference scores in rare, frequent and all conditions together (i.e. number of total correct pronunciations after context minus the total number of correct pronunciations before the context) revealing no differences between groups, that is, the position of the context had a similar effect in both groups (all Mann-Whitney  $U > .774$ , all  $p > .24$ ).

Most of the significant results reported above maintained their formal significance after correction for multiple testing (see Table 5.3).

#### **5.6.2.6 Additional aspects of cognitive performance**

Analysis of additional information obtained from the performance of participants on the Rey-Osterrieth Complex Figure Test is described below and the results are displayed in Table 5.4.

The BN group was less accurate in copying and recalling the complex figure. Also, they showed a lower percentage of recall relative to the HC group. Because the percentage of recall represents the scores in accuracy recall corrected by the scores obtained in accuracy copy, this indicates that the proportion information lost after the interval was significantly lower in BN relative to the HC group independently from the initial disadvantage in accuracy showed by the former group.

Women with BN, differing from what has been reported in Chapter 6 in AN, were not extremely impaired in organisational strategies as only a trend in comparison with the HC group was found ( $p = .09$ ). These results are in discrepancy with the significant difference between groups found in the central coherence indices, the main measure of drawing style used in this study.



**Table 5.3 Between groups comparison results in neuropsychological tasks that benefit from global processing**

		<b>BN</b> <i>n</i> = 42	<b>HC</b> <i>n</i> = 42	<b>Test statistic</b>		<i>p</i> -value	<i>d</i>	<b>AN *</b> <i>n</i> = 42	<i>p</i> -value	<i>d</i>
				<b>t-test<sup>a</sup></b>	<b>MW<sup>b</sup></b>					
RCFT COPY	order	2.2 (0.5)	2.5 (0.4)	-3.03	n.a.	.003 <sup>c</sup>	.66	2.1 (0.6)	.23	.18
	style	1.4 (0.5)	1.7 (0.3)	-2.8	n.a.	.005 <sup>c</sup>	.66	1.3 (0.5)	.48	.20
RCFT CC index copy		1.4 (0.4)	1.6 (0.3)	-3.35	n.a.	.001 <sup>c</sup>	.57	1.29 (0.4)	.30	.28
SCT local processing score		2 (1-3)	0 (0-1)	n.a.	424.5	<.001 <sup>c</sup>	1.07	1 (0-2)	.15	.32
SCT number of local completions		0 (0-1)	0 (0-0)	n.a.	737.0	.06	.20	0 (0-0)	.22	.26
HRT total score		15 (13-16)	15 (14-16)	n.a.	668.0	.047	.45	15 (14-16)	.09	.38

RCFT: Rey-Osterrieth Complex Figure; SCT: Sentences Completion Task; HRT: Homograph Reading Test

\*= AN results (for details see chapter 6) and pairwise comparison results between AN and BN

t-test<sup>a</sup>= t test statistics for t-test pairwise comparisons for data normally distributed, *M* and *SD* are displayed

MW<sup>b</sup>= U test statistics for Mann-Whitney *U* for data not normally distributed, *Mn* and upper and lower quartiles (*Q* 25-*Q* 75) are displayed.

na = not applicable.

<sup>c</sup> = Results that remained significant ( $p < 0.05$ ) after Hochberg correction for multiple testing (Hochberg, 1988).

#### 5.6.2.7 *An examination of potential mediators in the difference between groups on visual memory using the Rey-Osterrieth Complex Figure Test*

It was of interest to examine the potential influence of drawing style on percentage of recall of the RCFT with the purpose of replicating the mediation effect found in the study of AN. Since there was no significant difference between groups in organisational strategies, only the coherence index was included in the examination of drawing style effect on non-visual memory in the RCFT.

Supporting the hypothesis, the mediation model testing (Kenny et al., 1998) showed that the difference between groups in percentage of recall was mediated by the coherence in the process of drawing. The direct model based on simple regression analyses showed that the 'Group' variable accounted for 6% of the overall variance ( $B = 7.4$ ,  $SE = 3.2$ ,  $st.\beta = .24$ ,  $t = 2.3$ ,  $p = .03$ ) in percentage of recall. The coherence index also had a direct effect on recall ( $B = 17.1$ ,  $SE = 4.9$ ,  $st.\beta = .36$ ,  $t = 3.5$ ,  $p = .001$ ,  $R^2 = .13$ ). In the multiple regression analysis, the coherence index maintained its effect on the percentage of recall ( $B = 14.9$ ,  $SE = 5.2$ ,  $st.\beta = .31$ ,  $t = 2.9$ ,  $p = .005$ ) whereas the effect of group fell to non-significant levels ( $B = 4.1$ ,  $SE = 3.3$ ,  $st.\beta = .14$ ,  $t = 1.2$ ,  $p = .22$ ). This model explained three times the amount of the variance in percentage of recall than the direct model ( $F_{(2,81)} = 6.9$ ,  $p < .002$ ,  $R^2 = .15$ ).

The Sobel test showed that this mediating effect was significant ( $t = 2.17$ ,  $p = .03$ ). There was no interactions between group and coherence index effects, that is, no moderator effects were found ( $F_{(1,84)} = 1.4$ ,  $p = .20$ ).

As accuracy in the copy trial was lower in the BN group in comparison with the HC group and was demonstrated to be a powerful predictor of the low recall accuracy in BN ( $B = .67$ ,  $SE = .17$ ,  $st.\beta = .52$ ,  $t = 3.9$ ,  $p < .001$ ), it was investigated as a potential mediator for percentage of recall. However, it failed to demonstrate a significant effect in the model ( $p > .05$ ).

**Table 5.4 Accuracy and organisational strategies in RCFT**

Rey-Osterrieth Complex Figure	BN	HC	Test statistic		<i>p</i> -value	<i>d</i>	AN *	<i>p</i> -value	<i>d</i>
	<i>n</i> = 42	<i>n</i> = 42	t-test <sup>a</sup>	MW <sup>b</sup>			<i>n</i> = 42		
Copy accuracy	26.4 (3.3)	30.9 (3.6)	-5.96	na	<.001 <sup>c</sup>	1.30	30.9 (3.0)	<.001	1.43
Recall accuracy	14.7 (4.3)	19.6 (5.7)	-4.42	na	<.001 <sup>c</sup>	.97	16.7 (5.6)	.07	.40
Percentage of recall	55.5 (13.9)	62.8 (15.8)	-2.24	na	.026	.50	53.7 (1.61)	.59	.40
Organizational Strategy	4.5 (3-6)	5 (3-6)	na	704.0	.09	.37	4 (2-5)	.19	.29

\*= AN results (for details see chapter 6) and pairwise comparison results between AN and BN

t-test<sup>a</sup>= t test statistics for t-test pairwise comparisons for data normally distributed, *M* and *SD* are displayed

MW<sup>b</sup>= U test statistics for Mann-Whitney *U* for data not normally distributed, *Mn* and upper and lower quartiles (*Q* 25-*Q* 75) are displayed.

na = not applicable.

<sup>c</sup> = Results that remained significant ( $p < 0.05$ ) after Hochberg correction for multiple testing (Hochberg, 1988).

### 5.6.3 Exploring relationship between demographic and clinical variables and neuropsychological performance

Correlation analyses between demographic, clinical and neuropsychological variables were performed in the BN only. Results of correlation analysis for HC group were described in Chapter 4. Only main outcomes of coherence assessment were examined in association with anxiety, depression and obsessive-compulsive symptom levels and demographic variables such as age, years of education and intellectual ability. Following the procedures described in Chapter 4, point-biserial Pearson's correlations were carried out with the transformed scores in the Sentence Completion and Homograph Reading tasks and the demographic and clinical variables.

#### ***5.6.3.1 Examining relationship between neuropsychological performance and demographic variables***

In the BN group, there was a negative association between the age of participants and the percentage of recall in the RCFT ( $r = -.31, p = .048$ ). Also, older participants spent more time finding the hidden figures in the EFT ( $r_s = .38, p = .01$ ). Finally, older participants were found to benefit more from pre-segmentation of designs in the BD task ( $r = .48, p = .001$ ).

The variables that significantly correlated with neuropsychological performance were examined as potential confounder variables in the differences between groups.

Only age fulfilled criteria for inclusion as covariate in a model to explain percentage of recall. The other potential confounders mentioned above were not eligible for inclusion in an analysis of covariance after failing to meet the specific assumptions associated with ANCOVA (normality and homogeneity of regression slopes).

Therefore, a one-way between groups analysis of covariance was conducted to compare the BN and HC group with regards to the percentage of recall on the RCFT. The independent variable was 'group', and the dependent variable was the percentage of recall. Age of participants was used as the covariate. The ANCOVA results indicated that differences between groups in the percentage of recall remained

significant after controlling for age ( $F_{(1,81)} = 4.83, p = .03$ , partial eta squared = .06). Thus, age had little effect on the mentioned difference.

### **5.6.3.2 Levels of co-morbid symptoms and use of medicines**

#### Levels of co-morbidity

Although the group with BN had higher indices of psychopathological symptoms of anxiety, depression and obsessive-compulsive disorders, the only co-morbid variable that was found to be associated with neuropsychological performance was anxiety.

Anxiety levels correlated negatively with all the process measures in the RCFT i.e. higher anxiety was associated with lower coherence index ( $r = -.34, p = .04$ ) and organisational strategies ( $r_s = -.32, p = .03$ ).

As anxiety has been associated with a focused cognitive style (Happé and Frith, 2006), it was of interest to clarify its role in the differences between groups in the coherence index of the RCFT.

As a result, anxiety was tested as a potential covariate in the difference between groups on the coherence index provided that the model fitted the assumptions for ANCOVA. Importantly, the group difference in the coherence index was no longer significant after controlling for scores on anxiety ( $F_{(1,80)} = .365, p = .55$ , partial eta squared = .005). The relationship between coherence index and anxiety was however low as indicated by a partial eta squared value of .10. In summary, these results show that anxiety explained part of the local processing bias shown by the BN group particularly in the RCFT. Identification of the role of anxiety on the coherence index led to the reconsideration of the mediation hypothesis of the latter on percentage of recall. A model replacing the coherence index with anxiety as a mediator of the group differences in percentage of recall was tested. However, anxiety did not fit the criteria required for a mediator ( $p = .11$ ).

ANCOVA analyses could therefore not be conducted to examine the effect of anxiety in either the organisational strategies or the errors in the HRT.

Neuropsychological performance did not correlate with levels of depression or obsessive-compulsive symptoms in any of the groups (all  $p > .05$ ).

### Effect of use of psychotropic medicines

As mentioned before, a sample of women with BN ( $n = 7$ ) was on medication at the time of testing.

The effect of medicines on neuropsychological performance was investigated by comparing the sub-groups on and off medication and no effects were found in all the coherence outcome variables (all  $p > .33$ , all effect sizes were low or negligible). However, the potential confounding effect of medicines cannot be totally ruled out as the number of participants taking medicines was small.

With respect to the additional outcome variables measured by the RCFT, medium effect sizes were found in accuracy recall ( $t = -1.66$ ,  $p = .11$ ,  $d = .68$ ) and percentage of recall ( $t = -1.04$ ,  $p = .33$ ,  $d = .60$ ) in favour of non-medicated BN which might suggest that the use of medication may have interfered with non-verbal memory. Once again, unequal and small sample sizes in the case of medicated women precluded the inference of any stronger conclusion.

#### **5.6.3.3 Clinical variables**

Clinical variables such as BMI, age of onset, and severity of illness indicated by the duration of the disorder and use of multiple purging methods were examined in relationship with cognitive performance.

In the BN group, duration of illness correlated negatively with percentage of recall in the RCFT ( $r = .34$ ,  $p = .03$ ) and positively with time spent in searching for the hidden shapes in the EFT ( $r_s = .32$ ,  $p = .04$ ).

The use of multiple purging methods was low but significantly associated with lower coherence index in the RCFT ( $r = .32$ ,  $p = .04$ ) and at a trend level with errors in the EFT ( $r = .30$ ,  $p = .051$ ).

BMI did not correlate with any neuropsychological measure in either group.

*A comparison between those with and without a lifetime diagnosis of anorexia nervosa*

Some researchers have argued in favour of subtyping BN according to AN lifetime diagnosis due to its relevance as a prognosis indicator and in terms of clinical characteristics (Eddy et al., 2008). Accordingly, the BN group was split into those who had previous history of at least 3 months of AN nervosa following the DSM-IV criteria ( $n = 18$ , 42.9%) and those who have never had a period of AN ( $n = 24$ , 57.1%), in order to further explore the potential effects of clinical diagnostic sub-categories.

The mean age of onset was 16.35 years ( $SD = 3.7$ ) for the group without previous AN and 15.9 years ( $SD = 3.6$ ) in the subgroup with previous history of AN. This difference was not significant ( $t = .35$ ,  $df = 39.1$ ,  $p = .73$ ). No differences were found in terms of duration of the illness ( $t = -.12$ ,  $df = 40$ ,  $p = .90$ ). Those with antecedent AN had lower BMI than those without ( $M = 20.71$ ,  $SD = 2.16$  versus  $M = 22.55$ ,  $SD = 2.2$ ,  $t = 2.7$ ,  $p = .01$ ). However, there was no difference in BMI between women with a history of AN and healthy women ( $p = .76$ ).

In terms of neuropsychological assessment, there was also a trend in some differences to emerge. The group with lifetime AN had a greater number of local completions in the SCT (Mann-Whitney  $U = 164.0$ ,  $z = -1.7$ ,  $p = .09$ ,  $d = .53$ ), obtained higher percentage of recall on the RCFT ( $t$ -test =  $-1.51$ ,  $p = .14$ ,  $d = .47$ ) and benefited less from segmentation in the BD (Mann-Whitney  $U = 154.0$ ,  $z = -1.6$ ,  $p = .10$ ,  $d = .52$ ) than the 'pure' BN subgroup. The differences in the others tasks were small or negligible (all effect sizes  $d$  below .30 and  $p > .19$ ).

*A comparison between those with and without a lifetime diagnosis of anorexia nervosa and healthy controls*

As the comparison between those with lifetime AN and those with 'pure' bulimia was not able to give much relevant information about group differences, a further analysis was made to compare the subtypes of BN and the HC group in order to explore in more detail whether there were any important changes in the cognitive profile demonstrated by the whole BN group. Results for coherence indices are shown in Table 5.5.

**Table 5.5 A comparison between ‘pure’ bulimia nervosa, bulimia nervosa with lifetime anorexia nervosa and the healthy control group**

	‘Pure’ BN <i>n</i> = 24	Lifetime AN <i>n</i> = 18	HC <i>n</i> = 42	$\chi^2$ <sup>a</sup> <i>df</i> =2	<i>p</i> -value	Between groups comparisons <sup>b</sup>
EFT medians	7.6 (4.3-12.7)	6.4 (4.8-8.5)	12.2 (7.9-15.3)	9.5	.009	HC>PBN=LAN (all <i>p</i> <.017)
EFT errors	0 (0-2)	1 (0-2)	1 (0-2)	2.7	.265	
EFT false claims	2 (1-3)	2 (1-2)	2 (0-3)	.79	.675	
BD benefit from segmentation	37.2% (30-46)	28.3% (24-39)	39 % (28-50)	5.1	.080	HC>LAN <i>p</i> = .03
RCFT order	2 (1.8-2.7)	2.3 (2.2-2.5)	2.5 (2.2-3)	7.9	.016	HC>PBN <i>p</i> =.008 HC>LAN <i>p</i> =.09
style	1.5 (1-1.8)	1.5 (1.3-1.8)	1.7 (1.5-1.8)	4.5	.106	
coherence	1.4 (1-1.7)	1.5 (1.2-1.7)	1.6 (1.5-1.8)	8.5	.015	HC>PBN <i>p</i> =.01 HC>LAN <i>p</i> =.04
SCT local processing	2 (0-2)	2 (1-3)	0 (0-1)	19.0	<.001	HC>PBN=LAN <i>p</i> < .001
HRT initial pronunciation	14 (13-16)	15 (13-16)	15 (14-16)	4.3	.119	

PBN: Pure Bulimia Nervosa; LAN: Lifetime Anorexia Nervosa; HC : Health Controls

<sup>a</sup> = Data does not fit the assumptions of parametric testing therefore Kruskal-Wallis Test was used. Median values and interquartile ranges displayed (Q25-Q75).

<sup>b</sup> = Mann-Whitney *U* Test pairwise comparisons with Bonferroni adjustments (*p* <.017)

Kruskal-Wallis were carried out due to the lack of normality in data distribution. Main differences between the results of this multivariate comparison and the pairwise comparison previously carried out with the whole BN group were the resulting absence of statistical difference in the style index of the RCFT and the uncovered significant difference in benefit from segmentation in the BD test between the lifetime AN group and the HC group. The former group demonstrated reduced advantage from segmentation in comparison with the HC and ‘pure’ BN group.



#### 5.6.4 Neuropsychological performance in bulimia nervosa and anorexia nervosa: similarities and differences

As mentioned before, Tables 5.2-5.4 display the results of the AN group (Chapter 4) along with the neuropsychological outcomes of the BN group from the present study with the objective of providing an idea about how these two ED are different or similar across the coherence outcomes.

The AN group consisted of 42 women equivalent in age, IQ and years of education to the BN group described here.

Some significant differences were found between groups.

The BN group was faster although less accurate in tasks that benefit from local or detail processing tasks. Thus they showed a significantly faster performance in both sub-test of the BD and made more false claims and errors in the Embedded Figure Test, all with medium to high effect sizes. Also they were faster in the EFT but this difference failed to reach formal levels of significance ( $p = .14$ ,  $d = .33$ ).

However, no differences were observed with regards to the difficulties in global processing in both, verbal and visual-spatial level. An exception was a statistical trend in the HRT whereby the BN group made more errors in the initial pronunciation of the homographs.

In terms of the additional cognitive aspects addressed in the RCFT test, women with BN proved to be less accurate in copy accuracy, with a large effect size and a trend was found in recall accuracy.

In summary the BN group displayed a good but less accurate detail focused style than that observed in AN. Thus although the balance between a local and global focus is similar in direction to that found in AN (i.e. weak central coherence), the process appears to differ in that in some tasks people with BN are less accurate in the trade off between speed and accuracy.

## **5.7 Discussion**

The aim of this case-control study was to examine the concept of central coherence in people with BN, to reveal whether this cognitive characteristic was relevant for this distinctive eating disorder diagnostic category, and to explore similarities and difference in the cognitive profile between BN and AN.

In summary, the primary hypothesis that women with BN would show weaker performance in tasks that require strengths in global processing and contextual integration (i.e. lower coherence indices in the Rey-Osterrieth Complex Figure although mediated by anxiety levels, higher local scores in the Sentence Completion Task and more errors in the initial pronunciation in the Homograph Reading Task) was supported by the results of this study. Also the second part of this hypothesis, which was that people with BN would show superior function or a bias towards detail focused processing, was also confirmed (i.e. much faster responses in the Embedded Figures Test, and the trend for a smaller relative advantage from segmentation in the Block Design).

Together these findings suggest that people with BN have weak central coherence.

It was also hypothesised that the general cognitive profile of those with current BN would be an intermediate between the functioning of the AN and HC groups. The results concerning this issue are however less clear. Women with BN did obtain intermediate scores on the visual-spatial coherence indices of the Rey-Osterrieth Complex Figure and yet were significantly different to the HC group. However, the difference was not significant as compared to AN. In the verbal domain the BN group showed more difficulties in processing information into context than both the AN and the HC group. Finally, the BN group performed faster than AN and HC in local processing tasks (EFT and BD) but with lower accuracy in relationship to the AN group only. It might be possible that the poor nutritional status in some degree obscured the excellence in local processing as has been seen in other studies in AN (Laesse et al 1990) due to severe biological alterations. For example, severely underweight individuals with AN might have reduced their motor response (Green *et al.*, 1996, Kingston *et al.*, 1996, Szmukler *et al.*, 1992), although this has not been consistently proved (Murphy *et al.*, 2002, Pieters *et al.*, 2003, Witt *et al.*, 1985).

The errors in several tasks shown by people with BN (more false claims and errors in the EFT, lower accuracy in the RCFT) contrast to the error-free response style in AN. These differences between BN and AN may result from a greater fear of mistakes in AN (Halmi *et al.*, 2000) or may be better explained by other phenotypes relevant to BN and not to AN, such as cognitive disinhibition (impulsivity) rather than representing actual differences in coherence.

The overall cognitive profile identified in the group with BN in comparison with both the AN and HC groups (low visual-spatial global processing but less extreme than in AN, low verbal global processing but more extreme than in AN and superior local processing but with less accuracy than in AN) provides a preliminary indication of the heterogeneous nature of the concept of coherence. Firstly, it might be possible that the underlying mechanisms for verbal and visual-spatial coherence (and also the auditory coherence although not explored here) differ and that therefore individuals have different degree of coherence in diverse domains. The idea of the domain heterogeneity in coherence was also suggested in Chapter 6 with regards to the possibility that people with AN would display poorer coherence in visual-spatial levels but not in verbal levels. It was also put forward by Frith and Happé (Happé, 1994) who have highlighted the need for exploring coherence across domains in order to examine whether coherence corresponds to a unitary concept. Secondly, the diverse profile in BN would also support the idea that weak global and strong local processing are not in a linear trade-off relationship as was argued by the earlier studies in coherence in autistic spectrum disorders and later revised by the main proponents of this theory (Happé and Booth, 2008, Happé and Frith, 2006).

Considering the proposition that those with BN would show a similar profile to those with binge-purge AN (BPAN), two aspects of the assessment are worth mentioning. The groups were alike in showing a better performance in visual coherence in the RCFT than the restricting AN group (RAN) although in both cases the difference failed to reach formal levels of significance. Similarly, the BN group and the BPAN obtained significantly lower scores in accuracy than the AN and HC, and RAN and HC groups respectively. However, the tendency for the BN group to be faster than both the AN and HC groups in the EFT was not found in the BPAN group. Therefore, some but not all of the results supported the hypothesis of similar profiles between the binge purging ED groups. Along the same lines, other studies have found that on the whole BPAN individuals have more in common with BN than with RAN (Claes *et al.*, 2006, Toner *et al.*, 1987).

Finally, the purported discrepancy in functioning in the coherence assessment between the groups with and without past AN was weakly supported by the data of this study. Overall, these two subgroups displayed comparable cognitive profiles.

### 5.7.1 Discussion of specific predictions on neuropsychological performance

All the formulated predictions based on the central coherence account regarding the performance of women with current BN as a whole, were endorsed by the data resulting from this study.

In relation to a superiority in local processing, women with BN were faster in the EFT than the HC group, as was the AN group. Noteworthy, the level of mistakes was similar to that seen in the comparison group even though the speed was nearly half. In line with the previous findings, those with BN benefited less from the pre-segmentation of designs in the BD although the speed performance was in this case comparable to the HC.

In terms of visual-spatial coherence (global processing) measured by the RCFT, the prediction that the BN group would perform poorer than the HC group was supported by the lower scores in all central coherence indices obtained by the clinical group.

Also, more errors were made by the BN group in comparison with the HC group in the verbal global tasks suggesting weaker integrative processing in both the SCT and the HRT. However, there was found a similar context effect on the performance of both the BN and HC groups when they were examined by separate analyses. Unexpectedly, those with BN attempted to correct themselves more frequently than those in the HC after errors in the pronunciation of the homographs (HRT). A possible explanation might be related to the perfectionist tendencies existing in the BN group (Anderluh *et al.*, 2003, von Ranson *et al.*, 1999) that may have been prompted after realisation of mistakes. According to central coherence theory this observation would suggest the spontaneous action of the individual's cognitive style characterised by a detail focus and the possibility of later overcoming the bias in information processing (Happé and Frith, 2006).

Taking into account the subsidiary data, the mediator role of the coherence index on percentage of recall was replicated whereas the mediator role of organisational strategies was not. This suggests that although organisational strategies and coherence indices are related concepts they do not represent the same functions and supports the argument in favour of a distinction of central coherence as a cognitive style from the executive functions (measured in this study by the use of organisational strategies). A similar distinction was demonstrated in people with

ASD using measures of central coherence on the one hand, and planning on the other hand in a drawing task (Booth *et al.*, 2003).

Lastly, it was expected that the BN group would be less accurate across tasks as a demonstration of higher cognitive impulsivity. The performance of individuals with BN in this study did show some signs that could be seen as demonstrations of impulsivity (e.g. less accuracy in the RCFT, more local completions in the SCT, more errors in the HRT in comparison with the HC group). However, some of them could be understood only as a result of a strong local bias, consistent with the weak coherence hypothesis. The exception would be the low accuracy in the RCFT. This was not seen in people with AN studied in comparison with the same HC group (Lopez *et al.*, in press). On the other hand previous studies in people with AN have found lower copy accuracy with effect sizes ranging from -0.18 to -1.5 (Kingston *et al.*, 1996, Mathias and Kent, 1998, Murphy *et al.*, 2002, Sherman *et al.*, 2006, Thompson, 1993) whereas the only other previous study in BN found no deficit in copy accuracy (Murphy *et al.*, 2002). Such low scores in copy accuracy as seen here have been reported in a few studies in people with schizophrenia (Sullivan *et al.*, 1992, Zanello *et al.*, 2006), alcoholism, those with lesions in the right parietal and frontal lobes (Sullivan *et al.*, 1992) and in overweight people (Roberts *et al.*, in press). However, most of the studies in other less damaged psychiatric populations e.g. in OCD (Moritz *et al.*, 2005, Penades *et al.*, 2005, Savage *et al.*, 1999, Shin *et al.*, 2004), body dysmorphic disorder (Deckersbach *et al.*, 2000), Tourette syndrome and other anxiety disorders (Lavoie *et al.*, 2007), have found no differences in copy accuracy with their respective control groups. Thus cognitive impulsivity could be one within several other possible hypotheses that could explain the lower accuracy in the BN group in comparison with the HC and AN groups. However, it is important to note that several studies have found no difference in cognitive impulsivity between ED groups (Rosval *et al.*, 2006, Southgate *et al.*, 2007). Other factors such as poor motivation, lack of attention, carelessness, lack of planning, behavioural impulsivity, etc., may also account for this. Replication of this study addressing aspects of cognitive impulsivity may help to clarify this effect.

### 5.7.2 Possible confounders

The influence of clinical and demographic variables on neurocognitive functioning was examined in this study. Overall, relationships were weak or non-significant.

The group with BN had higher indices of co-morbid symptoms that may have influenced the results in this study. As mentioned before, only weak relationships were found between clinical variables and cognitive coherence. The main exception was the role of anxiety on the low general coherence index of the RCFT in BN that was able to explain the differences between groups on this variable but only a minimum part of the variance of the coherence index. Anxiety has been associated with weak coherence (Happé and Frith, 2006) and is also highly present in individuals with BN (Kaye *et al.*, 2004). Since the group of women with BN had a long history of the illness, it is hard to isolate the effect of anxiety from their cognitive functioning. Even when anxiety made the difference between BN and HC groups negligible in the coherence index, it did not have an important role in any other of the weak coherence tendencies showed by the BN group across tasks.

In terms of severity of the illness, multiple purging methods but not length of the illness was related to fewer errors in the EFT. No other relationships were found across the different tasks. Previous studies have found no effect of illness severity and neuropsychological performance in BN (Bowers, 1994, Laessle *et al.*, 1990).

The effect of the use of medicines on coherence variables could not be fully discarded, as the sample sizes of those on medication were very small. It is possible to argue then that the results obtained here are generalisable to the majority of women with BN without medication. However there was some indication that those on medication performed poorer in other aspects of the tasks (accuracy and percentage of recall).

It is worthy to note that after splitting the BN according to their lifetime AN, those in the subgroup with a preceding history of AN had a lower mean BMI than those who have never had AN. Similar results have been previously found in cross-sectional studies (Eddy *et al.*, 2008) and may have implications on cognitive functioning. However, no effect of BMI on any task was found in this study. A previous study found that current BN patients with a previous history of AN performed poorer on neuropsychological testing than those without such antecedent

history, suggesting that the previous period of starvation might have long term consequences on cognitive functioning (Laessle et al., 1990). This observation has not been replicated and contradicts the results found in this study and in the majority of the studies in AN wherein the nutritional status as indicated by current BMI has not been found to be related with neuropsychological impairment (e.g. Bowers, 1994, Murphy *et al.*, 2002).

### 5.7.3 Limitations of the study

This study has some limitations. Firstly, a large proportion of this clinical sample had a previous episode of AN and it might therefore be expected that the endophenotype in this group would closely resemble that of AN. Also, it has been argued that the absence or presence of a period of AN in the lifetime relates to a series of differences in terms of prognostic and clinical factors that highlight the importance of looking at these two subgroups separately (Eddy et al., 2008). A larger sample size would be needed to explore this hypothesis further. Secondly, additional tasks to examine confounding features such as a reflective versus a disinhibited/impulsive cognitive style and set-shifting may allow a more complete characterisation of the neuropsychological profile in BN. Thirdly, some of the BN participants were on medication at the time of the study. However, no evidence that medication would affect performance in coherence variables was found. Fourthly, as acknowledged in Chapter 4, a third of the HC did not complete an assessment of level of intellectual ability. However, no major associations were found between intellectual levels and neuropsychological performance and it was not expected that the group without the assessment was significantly different from those who had the assessment since they were equivalent in terms of years of education which is in general a good predictor of intelligence (Lezak *et al.*, 2004). Finally, it would be of interest to study people with binge eating disorder and purging disorder to examine whether they also have weak central coherence.

#### 5.7.4 Strengths of the study

Some strengths of this study are worth mentioning. First, one of the main strengths of this study is the large number of participants with BN which exceed samples used in most of the previous studies looking at the neuropsychological functioning in this group, particularly in the area of global/local processing (McLaughlin *et al.*, 1985, Murphy *et al.*, 2002, 2004, Pendleton Jones *et al.*, 1991, Southgate *et al.*, 2007). The current sample size also enabled the examination of differences according to lifetime diagnoses. Secondly, it was fruitful to pursue the comparison of cognitive functioning between those with BN and AN and between those with BN and binge-purge subtype of AN, in a range of neurocognitive tasks. Thirdly, methodological procedures allowed controlling for some of the clinical variables that might have influenced cognitive performance. Finally, a large number of BN participants were recruited from the general community which was expected to provide a profile much closer to what it is possible to find in the heterogeneous population with BN and prevent selection bias especially in a group that is known for avoiding to seek help (Fairburn and Harrison, 2003).

#### 5.7.5 Clinical and research implications of these findings

Behavioural expressions of weak coherence in BN appear to be less evident than in AN perhaps because this disorder has been more typically associated with an impulsive behavioural profile which seems to be far from a tendency for attention to detail, as the weak coherence account would claim. It seems easier then to link weak coherence with both the ‘perfectionist’ and ‘compulsive’ (overregulated) rather than with the ‘dysregulated’ sub-phenotype of BN (Steiger and Bruce, 2007). However it could be argue that it is also linked to the broader spectrum of BN as seen in this study.

Weak central coherence may underpin some of the clinical characteristics seen in people with BN and interact with others. This tendency to get trapped by details may trigger behavioural and cognitive traits of bulimia nervosa such as obsessiveness (persistent concerns about weight and shape), and compulsivity (e.g. uncontrollable binge and purge behaviours) which are known to persist even after recovery (von Ranson *et al.*, 1999). Also difficulties in global processing, as part of the endophenotype of weak coherence, may interact with impulsivity or problems



with response inhibition (e.g. difficulty to analyse pros and cons in the ‘urge’ of the stress), and the apparent difficulty to integrate their illness in the continuum of their lifetime manifested in the so called ‘risky-taking attitude’ (Rosval et al., 2006) hindering the possibility of contemplating the long-term consequences of the unhealthy methods to control weight (e.g. vomiting, use of laxatives and diuretics).

The results from this study open the possibility of including cognitive remediation within the treatment for people with BN in addition to people with AN. In the same form that this information can be integrated into clinical interventions for AN, psychotherapeutic interventions in BN may need to help patients to be aware of the effects of this information processing bias and encourage the reflection on and improvement of contextual integration into the global aspects of the life story. Specific treatment modules of interventions to strength global processing abilities might also be of value but most of the available research so far have been focused on AN (Lopez *et al.*, 2008a, Tchanturia *et al.*, 2007a, Tchanturia *et al.*, 2008). For example, a motivational feedback based on neuropsychological assessment has been found to be helpful in a small sample of women with ED with different diagnostic categories (see Chapter 9).

The relevance of training people with ED in the use of global strategies and to compensate the detail bias has its rationale in the hypothesis that a predominant detail focus style in both AN and BN may interfere with adapting to the unpredictable changes of daily life and the challenges entailed in normal psychosocial development. Shah and Frith (Shah and Frith, 1993) acknowledged that while the strength in faster processing of unconnected information and dividing of wholes into their parts was advantageous ‘in lab’ tasks for some people with autism, a normal daily life does not usually require this ability. In fact, the information processing in real life in general requires the ability to achieve coherence from individual pieces of information. The same could be argued for the difficult process of recovery. It could be interesting to investigate how weak coherence relates to treatment outcomes and prognosis and whether there is any effective difference within the sub-phenotypes of BN in this aspect of cognitive functioning.

These findings reinforce the possible link between ED and ASD in terms of cognitive functioning (Gillberg *et al.*, 2007). Since the phenotypical characteristics of those with BN and ASD seem to be little related it might be interesting to investigate further both the gene-environment contributions and the neurobiological substrate of

weak coherence. Studies using imaging might help not only to uncover the mechanism behind global and analytical abilities which is still uncertain (Happé and Frith, 2006) but also to better understand the similarities and differences between subtypes of ED and other disorders presenting weak coherence, and in particular ASD.

The specific mode in which weak coherence relates to other aspects of functioning in bulimic disorders (e.g. sensitivity to reward, impulsivity, compulsivity) needs further examination.

In spite of these uncertainties, the conclusions from this study may contribute to a better understanding of how people with BN think and learn.

## **5.8 Conclusion**

In summary, weak central coherence seems to be a cognitive style characteristic of women with bulimia nervosa. This group showed a cognitive profile in line with all the predictions set forth by the central coherence hypothesis. Thus, weak contextual integration was evident across domains (verbal and visual-spatial) and there was also evidence of enhanced detail functioning in this group.

The neuropsychological profile identified in people with bulimia nervosa shows similarities with that seen in women with current anorexia nervosa. However, there are a few differences in the profile of their respective central coherence test results that merit further examination. This may represent a difference in the central coherence endophenotype between bulimia nervosa and anorexia nervosa or it may be that other factors may moderate the results (e.g. anxiety).

This study gives evidence in support of the argument that independent of the predominant diagnostic category both anorexia nervosa and bulimia nervosa share a cognitive bias towards detail. Consequently these findings would indicate that anomalies in information processing such as weak coherence are independent of the starvation status typical of those with anorexia nervosa. Finally, the findings of this study open the possibility of exploring this cognitive style further as a possible endophenotype candidate for eating disorders. The next step is to examine coherence in people who meet criteria for long-term recovery from an eating disorder.

## **6 WEAK CENTRAL COHERENCE IN WOMEN RECOVERED FROM AN EATING DISORDER: STATE OR TRAIT EFFECT? <sup>8</sup>**

### **6.1 Introduction to the chapter**

This chapter presents the final step in the preliminary exploration of weak central coherence as an endophenotype candidate for eating disorders (ED). According to Gottesman and Gould's review of the concept of endophenotypes in psychiatry research, an endophenotype should be independent of the active state of the illness (Gottesman and Gould, 2003), in other words, it should be present in individuals recovered from the disorder under study.

This chapter explores whether women who are recovered from an eating disorder (EDRec) display a cognitive profile in line with the weak central coherence hypothesis.

### **6.2 Background and development of the study**

The work previously described in Chapters 4 and 5, showed that women with anorexia nervosa (AN) and bulimia nervosa (BN) have weak coherence. From the endophenotypic conceptualisation, these findings represent the most basic assumptions relative to the association between a potential endophenotype and the illness (Gottesman and Gould, 2003). The following step would be to identify whether the endophenotype candidate is 'primarily state-independent' (Gottesman and Gould, 2003, pp. 639). This criterion can be explored in several ways: (1) ideally, a longitudinal study of a population at risk of developing the illness would show that those who will develop the disorders would display the trait before the illness becomes active and also during periods of remission, (2) eliciting the endophenotype by a trait challenge i.e. in someone who does not manifest the illness the trait can be provoked to become observable (e.g. glucose tolerance test in

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<sup>8</sup> A version of this chapter has been published as a research article in the Journal of Clinical and Experimental Neuropsychology as 'Weak central coherence in eating disorders: A step towards looking for an endophenotype of eating disorders' (Lopez *et al.*, 2008)

unaffected relatives of an individual with diabetes) (Gould and Gottesman, 2006), (3) employing a cross-sectional study that examines the existence of the trait once the illness is not present assuming that enduring traits which are present after recovery are pre-morbid (i.e. in recovered samples). Acknowledging the limitations that employing a recovered group may involve, the latter method, supplemented with a comparison with an equivalent healthy control group, was used in the study described here. The method of including recovered or asymptomatic individuals to explore potential endophenotypes has been used before in the examination for other psychiatric disorders (Hasler et al., 2006). In ED, recovered samples have been used in studies of personality features (e.g. Lilenfeld *et al.*, 2000, Matsunaga *et al.*, 2000, Wagner *et al.*, 2006a), persistence of typical co-morbid symptoms (e.g. Holtkamp *et al.*, 2005, von Ranson *et al.*, 1999), cognitive functioning (e.g. Bosanac *et al.*, 2007, Tchanturia *et al.*, 2004c, Tchanturia *et al.*, 2007b, Wagner *et al.*, 2007), and biologic markers (e.g. Bailer *et al.*, 2007, Wagner *et al.*, 2008, Wagner *et al.*, 2006b). It is assumed that the identification of enduring traits would indicate their presence prior to the development of the illness (Kordy et al., 2002).

Overall, the study of long-term recovered populations is relatively limited and new in the eating disorders field with an interesting increase in the last 10 years. Many studies have, however, looked into the effect of weight recovery (partial or total) on different facets of anorexia nervosa, and particularly on cognition and brain functioning (e.g. Bradley *et al.*, 1997, Green *et al.*, 1996, Kitabayashi *et al.*, 2004, Tchanturia *et al.*, 2002). Particularly relevant for this thesis is the longitudinal study of a cohort of early onset AN in a Swedish community sample conducted by Christopher Gillberg and collaborators, which has been described in previous chapters (Gillberg *et al.*, 1994a, Gillberg *et al.*, 1996, Gillberg *et al.*, 2007, Rastam *et al.*, 1997, Råstam *et al.*, 2003). In their last study, these authors described the executive and cognitive functioning of their sample, most of them recovered, after 10 years from the onset (Gillberg *et al.*, 2007) and found similar a cognitive profile displayed by the AN group over time, which differed minimally from HC. Mainly, this partially recovered AN group showed difficulties in the Object Assembly task which requires solving small jigsaw puzzles of familiar objects.

Although some studies have explored cognitive functioning in ED recovered samples, very little has been done in the study of global versus local cognitive strategies in this group and nothing, as far as we are aware, towards directly

exploring the concept of central coherence. The systematic review found only one research article that included a fully-recovered group in a comprehensive neuropsychological study looking at attention, concentration and vigilance, which involved the use of three tasks that may relate to local and global functioning (Pendleton Jones et al., 1991).

### **6.3 Aims**

The main aim of this study was to examine whether weak coherence, in terms of both superior detail processing and a weakness for global integration, was present in people with a past history of ED, currently recovered (EDRec). Thus, the study constitutes a further step in the examination of weak coherence as an endophenotype for eating disorders. A secondary aim was to contribute to the current knowledge about cognitive functioning of individuals who have reached recovery from an eating disorder.

### **6.4 Methods**

#### **6.4.1 Study design:**

The study described here employed a cross sectional case-control design.

#### **6.4.2 Participants:**

Forty-two women long-term recovered from an eating disorder (AN or BN) were recruited for this study. This recovered group (EDRec) was compared with a healthy control group (HC). The EDRec and HC groups were equivalent in sex, age and intellectual ability. A general description of the samples is given below. Full demographic information is provided later in the chapter (see Results section).

##### ***6.4.2.1 Participants recovered from an eating disorder:***

The recovered group (EDRec), as described in Chapter 3, was defined as women who had a history of AN or BN according to the DSM-IV diagnostic criteria but had no remaining symptoms in the current year (no bingeing, purging, food restriction or excessive exercise for at least 12 months) and who had also maintained

a Body Mass Index within a healthy range for at least a year (BMI between 19 and 26 kg/m<sup>2</sup>). Additionally, they needed to be free of psychotropic medicines in order to participate in the study in order to prevent potential confounding effects of medicines and/or severe psychopathological conditions.

The lifetime diagnosis was made based on the semi-structured EATATE interview (Anderluh *et al.*, 2008, Anderluh *et al.*, 2003). This interview produces a description of eating disorder symptoms over the life course (symptomatic periods, periods of remission and relapse, and examination of symptoms fluctuation per each core ED symptom), which in this study helped to determine the status of recovery of our participants with relative accuracy.

This EDRec group were fully recovered women who had not taken part in the previous study in AN described in Chapter 4. They were recruited from the general community via web-site advertisements ( $n = 20$ , 47.6 %), the staff ( $n = 6$ , 14.3 %) and the student population of King's College London ( $n = 10$ , 23.8 %) and from the volunteer database held at the Eating Disorders Unit of the Institute of Psychiatry ( $n = 6$ , 14.3 %).

#### *Establishing main lifetime diagnosis*

Due to the high instability of the diagnostic categories over the course of the disorder (Eddy *et al.*, 2008, Tozzi *et al.*, 2005), the full range of ED symptoms presented throughout the course of the illness was taken into account in order to determine the 'main' lifetime diagnostic. The 'main' lifetime diagnosis was defined as the most stable diagnostic category during the course of the illness according to the DSM-IV diagnostic criteria. That is, if an individual had periods of both AN and BN they would be given a main diagnosis according to the proportion of time during which they were ill and fulfilling any of the two diagnostic categories. If both diagnostic categories were comparable in terms of time the hierarchical approach used by the National Institute of Mental Health (NIMH) 'Genetics of Anorexia Nervosa study' was used (Kaye *et al.*, 2008). In this approach, binge eating 'trumps' purging and this supersedes restriction, therefore when AN and BN coexist BN takes predominance or priority over of AN.

The range of possible diagnostic categories is shown in. The Table 6.1 also shows the proportion of EDRec women in this study falling within each main

diagnostic category. According to the criteria described above, 35 women had AN (83.3%) and 7 had BN (16.6%) as their main lifetime diagnosis. A total of 37 women EDRec (88.1%) had a period of AN at some point of their lives.

**Table 6.1 ‘Main’ lifetime diagnostic categories**

Main lifetime diagnosis	Criteria	<i>n</i> (%)
RAN	Predominant restricting subtype of AN according to DSM-IV with no lifetime binge eating or purging	14 (33.3 %)
PAN	Predominant purging subtype of AN according to DSM-IV with lifetime purging but not bingeing	9 (21.4 %)
BPAN	Predominant binge and purge subtype of AN with persisting low weight (not fulfilling criteria for BN, BMI > 17.5)	12 (28.6 %)
PBN	Predominant lifetime of BN according to DSM-IV or equivalent time suffering from BN and AN	5 (11.9 %)
NPBN	Predominant lifetime of BN according to DSM-IV with bingeing but without purging behaviours	2 (4.8 %)

#### 6.4.2.2 *Healthy control participants*

The healthy control group (HC) was the same sample as used in our previous studies of coherence (see Chapters 4 and 5). The inclusion criteria for healthy controls included a BMI between 19 and 26 (kg/m<sup>2</sup>), no psychoactive medicines and no personal or family history of ED or any other psychiatric illness.

#### 6.4.3 Measures

A full description of the measures utilised in this study is provided in Chapter 3. The assessment battery has been described previously in Chapters 4 and 5.

As the most common concurrent conditions of ED such as depressive, anxiety and obsessive compulsive symptoms may persist after recovery (Gillberg *et al.*, 1995, Holtkamp *et al.*, 2005, von Ranson *et al.*, 1999) and can also influence cognitive functioning (Castaneda *et al.*, 2008, Kuelz *et al.*, 2004), symptom levels were assessed in this study using the *Hospital Anxiety and Depression Inventory*

(HADS) (Zigmond and Snaith, 1983) and the *Obsessive Compulsive Inventory-Revised* (Foa *et al.*, 2002, Foa *et al.*, 1998).

#### 6.4.4 Procedure

The same procedures as described in the studies exploring central coherence in AN and BN were used in this study. Weight and height were measured on the day of testing. All the neuropsychological measures were administered in the same order: RCFT (copy), SCT, EFT, HRT, RCFT (recall), Un-segmented Block Design, EATATE interview and Segmented Block Design. Questionnaires were completed a week before or after the testing session. The NART test was not obtained from the first 18 participants (three from the BN group and 15 of the HC group). One woman in the EDRec group and one in the HC group did not return the HADS questionnaire and 3 in the EDRec group also did not return the OCI-R self-report measure. Their data were nevertheless included in the analyses of the main outcome measures (central coherence battery).

#### 6.4.5 Data Analysis

The same data analysis procedures as described in Chapter 4 and 5 were used in the present study.

### **6.5 Hypotheses and Predictions**

The main hypothesis was that weak coherence would be an endophenotypical trait underpinning the development of ED and, as such, would be independent of acute illness state. Therefore it was expected that women recovered from an eating disorder, as a whole, would have weak coherence (i.e. enhanced detail processing and weak global processing) to a higher degree than a healthy control sample.

A subsidiary hypothesis was that the general cognitive profile of women with main lifetime diagnosis of AN might differ from the profile displayed by those with main lifetime diagnosis of BN. Therefore it was expected that a comparison between the whole EDRec group and the healthy control group would yield somewhat different results before and after excluding those with main lifetime diagnosis of BN



### 6.5.1 Predictions about neuropsychological performance based on the central coherence account

According to the central coherence theory, the following predictions with regards to the cognitive performance on the central coherence battery of tests were made. Women in the EDRec group would:

- Be faster and more accurate than HC in identifying the hidden figures in the Embedded Figure Test (EFT).
- Benefit less from segmentation of the designs in the Block Design Task (Un/seg BD).
- Display lower central coherence indices in the Rey-Figure Complex Test (RCFT) relative to the HC.
- Make more errors in the initial pronunciation of the homographs in the Homograph Reading Task (HRT) with decreased use of context and would show more difficulties than the HC in finding appropriate (with relevance to the sentence context) answers to the Sentence Completion Task (SCT).

In other aspects of the tasks, group differences in percentage of recall in the RCFT would be expected due to the effect of drawing style (coherence indices) on non-verbal memory. Percentage of recall would therefore be partly explained by drawing style.

## **6.6 Results**

### 6.6.1 Demographic and clinical characteristics

The results of demographic and clinical characteristics are shown in Table 6.2.

The EDRec group consisted of 35 women who had a history of AN (83.3%) and 7 who had BN as their main lifetime diagnosis. Thirty-seven out of the 42 EDRec group (88.1%) had a period of AN at some point of their lives. The mean age of onset was 16.1 years ( $SD = 3.9$ ) and their mean duration of illness was 6.1 years ( $SD = 4.6$ ).

The EDRec group had higher levels of anxiety, depression and obsessive – compulsive symptoms than the HC group (see Table 6.2). None of the participants in this group were on medication.

The EDRec group was comparable to the HC group in terms of age, years of education, and estimated intellectual ability (all  $p > .05$ ).

Although the EDRec group was recovered for a considerable length of time ( $M = 6.4$  years,  $SD = 5.75$ ), their BMI was still lower than the mean BMI of the HC group ( $t_{(82)} = .21$ ,  $p = .03$ ).

**Table 6.2 Demographic and clinical characteristics of EDRec and HC groups**

	<i>n</i>		EDRec	HC	Test	statistic	<i>p</i> -value	Effect
	EDRec	HC			t-test <sup>a</sup>	MW <sup>b</sup>		Size ( <i>d</i> )
Age (years) <sup>b</sup>	42	42	25 (21-31)	26 (22-29)	n.a.	858.5	.83	.04
Number of years of education <sup>b</sup>	41	42	16 (14-18)	17 (14.7-19)	n.a.	432.0	.12	.32
Estimated Intellectual ability <sup>a</sup>	39	27	113. (5.3)	112.2 (5.4)	-1.08	n.a.	.28	.26
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	42	42	20.9 (2.2)	21.9 (2.7)	.211	n.a.	.03	.41
Anxiety HADS <sup>a</sup>	41	41	9.9 (3.0)	6.0 (3.2)	-5.67	n.a.	<.001 <sup>c</sup>	1.26
Depression HADS <sup>b</sup>	41	41	9.0 (7-9)	2.0 (1-3)	n.a.	52.5	<.001 <sup>c</sup>	2.5
OCI-R <sup>b</sup>	39	42	16 (9-25)	6.5 (3-10)	n.a.	307.5	<.001 <sup>c</sup>	1.25

<sup>a</sup> *t*-test = test statistics for *t*-test pairwise comparisons for data normally distributed, mean values displayed with standard deviations.

<sup>b</sup> MW = test statistics for Mann-Whitney *U* for data not normally distributed, median values displayed with upper and lower quartiles.

na = not applicable.

<sup>c</sup> = Results that remained significant after Hochberg (Hochberg, 1988) corrections for multiple testing ( $p < .05$ )

## 6.6.2 Neuropsychological Function

The results from tasks thought to benefit from detail processing of information are displayed in Table 6.3.

**Table 6.3 Neuropsychological tasks that benefit from a detail focused processing**

	<b>EDRec <i>n</i> = 42</b>	<b>HC <i>n</i> = 42</b>	<b>Test statistic</b>		<b><i>p</i>-value</b>	<b>Effect Size (<i>d</i>)</b>
			<b><i>t</i>-test</b>	<b><i>MW</i></b>		
EFT total time taken (medians) <sup>b</sup>	6.7 (3.7-10.2)	12.2 (7.9-15.3)	na	419.0	<.001 <sup>c</sup>	1.01
EFT number time-out failures <sup>b</sup>	0 (0-1)	1 (0-2)	na	560.0	.002 <sup>c</sup>	.72
EFT false claims <sup>b</sup>	1 (0-2)	2 (0-3)	na	647.5	.03	.49
Un-segmented Block Design <sup>b</sup>	47.3(38.1-66.0)	44.9 (36.5-62.7)	na	875.0	.95	.01
Segmented Block Design <sup>b</sup>	28.9 (24.7-33.1)	27.7 (25.5-31.5)	na	826.5	.62	.11
Benefit from Segmentation <sup>a</sup>	38.3 % (14.9)	40.9 % (16.3)	.74	na	.46	.17

Note: Legends as previous table

<sup>c</sup> = Results that remained significant ( $p < .05$ ) after Hochberg correction for multiple testing (Hochberg, 1988)

### 6.6.2.1 Embedded Figures Test

Participants recovered from an ED excelled in this task as they were able to identify the hidden figures faster, and completed more items than the HC group within the time limit. They also made fewer false claims during the task, demonstrating better accuracy.

### 6.6.2.2 Un-Segmented Block Design Task

No differences were found in both the un-segmented and segmented parts of the Block Design Task in terms of time spent constructing the replicas of the designs and in the percentage of advantage when designs were segmented.

In terms of global processing, the EDRec group performed generally poorer than the HC group. Results from the tasks thought to benefit from integrative processing of information are shown in Table 6.4.

**Table 6.4 Neuropsychological tasks that benefit from global integration**

		<b>EDRec</b> <i>n</i> = 42	<b>HC</b> <i>n</i> = 42	<b>Test statistic</b>		<b><i>p</i>-value</b>	<b>Effect Size (<i>d</i>)</b>
				<i>t</i> -test	<i>MW</i>		
RCFT	order <sup>a</sup>	2.2 (0.7)	2.5 (0.4)	2.01	na	.05	.53
	style <sup>a</sup>	1.4 (0.5)	1.7 (0.3)	3.30	na	.002 <sup>c</sup>	.73
	coherence <sup>a</sup>	1.4 (0.4)	1.6 (0.3)	3.03	na	< .001 <sup>c</sup>	.57
SCT local processing score <sup>b</sup>		1.5 (1-3)	0 (0-1)	Na	391.0	< .001 <sup>c</sup>	1.15
SCT number of local completions <sup>b</sup>		0 (0-0)	0 (0-0)	Na	819.0	.370	.18
HRT total score <sup>b</sup>		15 (14-15)	15 (14-16)	Na	691.5	.08	.39

Note: Legends as previous table

<sup>c</sup> = Results that remained significant ( $p < .05$ ) after Hochberg correction for multiple testing (Hochberg, 1988).

### 6.6.2.3 *Rey-Osterrieth Complex Figure Test*

The EDRec group showed poorer global integration in the drawing process of the RCFT relative to the HC group, with low scores on all the coherence indices (style, order of construction and coherence index). The main difficulty showed by the EDRec group related to the high fragmentation in the drawing style.

### 6.6.2.4 *Sentence Completion Task*

The EDRec group obtained a higher local processing score, as they took longer to give an appropriate completion to the sentences. There was no difference between groups in the number of local completions which were in general, infrequent. Following guidelines from Happé and collaborators (2001), participants

were divided into groups showing good and poor performance on this task. In the EDRec group, 50% showed a poor performance (one or more local completions and/or two or more long hesitations) whereas in the HC group only 16.7% fell in that category ( $\chi^2 = 10.5, p = .001$ ).

#### **6.6.2.5 Homograph Reading Task**

The EDRec group made more errors in the initial pronunciation of the homographs but this difference did not reach formal levels of significance ( $p = .08$ ).

None of the participants showed difficulties reading the homograph from the pre-test list. No significant differences were found between groups in the total initial pronunciation score and across the four homograph conditions. Only a trend towards significance was found in the before – rare condition wherein the HC group made fewer errors reading the homographs (Mann-Whitney  $U = 715.0, z = -1.69, p = .09, d = .37$ ). Also, there was a trend towards statistical difference in the total number of individuals within groups that made errors in the initial pronunciation of the homographs (EDRec = 78.6%, HC = 59.5%,  $\chi^2 = 3.6, p = .06$ ).

As seen in the previous studies involving ED groups, there was a higher percentage of women in the EDRec group who made self-corrections after mistakes in the pronunciation of the homograph (EDRec = 81.8 % versus HC = 16 %) reaching a statistically significant level ( $\chi^2 = 24.7, p < .001$ ). The examination of the effect of context position using Wilcoxon's Signed Ranks Tests within each group for rare and frequent pronunciations revealed that both the EDRec and HC groups improved their performance when the context preceded the homograph in the rare condition (after-rare versus before-rare conditions: EDRec:  $z = -2.69, p = .007$ ; HC:  $z = -2.18, p = .03$ ). However, in the frequent pronunciation of the homograph, the context position was relevant only for the EDRec group (after-frequent versus before-frequent: EDRec:  $z = -1.96, p = 0.05$ ; HC:  $z = -1.21, p = .23$ ).

Finally, individual effects of sentence context for initial pronunciation were examined using the difference score (total number of correct pronunciations in sentences where the context preceded the homograph minus total number of correct pronunciations in sentences where the context followed the homograph). This analysis revealed no differences between groups for general context effect across all type of homographs and in the rare or frequent conditions (all Mann-Whitney  $U >$

815.0, all  $p > .38$ , all  $d < .18$ ). Therefore, the influence of context position in the accuracy of the initial pronunciation was similar in both the EDRec and HC groups.

Together these findings indicate that the EDRec group had more difficulties in global integration at both visual-spatial and verbal levels in comparison with the HC group and excelled in at least one task that favoured from local processing.

#### 6.6.2.6 Additional aspects of cognitive performance

Additional aspects of the cognitive processing were obtained from the Rey-Osterrieth Figure Test (ROFT). The EDRec group obtained poorer scores in copy ( $t_{(82)} = 6.9, p < .001$ ) and recall accuracy ( $t_{(82)} = 3.7, p < .001$ ) in comparison with the HC group. However, no significant differences were found in the percentage of recall or in organisational strategies.

This supplementary information about cognitive functioning is displayed in Table 6.5.

**Table 6.5 Accuracy and organisational strategies in RCFT**

	<b>EDRec <i>n</i> = 42</b>	<b>HC <i>n</i> = 42</b>	<b>Test statistic</b>		<b><i>p</i>-value</b>	<b>Effect Size (<i>d</i>)</b>
			<b><i>t</i>-test</b>	<b><i>MW</i></b>		
RCFT copy accuracy <sup>a</sup>	25.9 (3.1)	30.9 (3.6)	6.9	n.a.	< .001	1.48
RCFT recall accuracy <sup>a</sup>	15.3 (4.9)	19.6 (5.7)	3.7	n.a.	< .001	.81
RCFT percentage of recall <sup>a</sup>	58.8 (16.3)	62.8 (15.8)	1.2	n.a.	.26	.25
Organisational Strategy <sup>b</sup>	5 (2-6)	5 (3-6)	n.a.	707.0	.10	.35

Note: Legends as previous table

All significant results remained significant ( $p < .05$ ) after Hochberg correction for multiple testing (Hochberg, 1988).

### **6.6.2.7 *The role of drawing style on visual memory seen in the RCFT***

As there was no difference between groups in the percentage of recall i.e. no differences in visual memory, it was not possible to conduct a mediation analysis

### **6.6.3 The effects of demographic and clinical variables on neuropsychological performance**

Correlation analyses to explore potential relationships between neuropsychological performance (coherence variables and demographic and clinical variables) were performed in the EDRec group only. Results for the HC group were presented in Chapter 4. Those variables that were found to be strongly related with neuropsychological functioning were explored further using analysis of covariance (ANCOVA) provided that the relevant assumptions for this type of analysis were met. All the correlations, however, were small. Only significant results in each group are described below.

As mentioned in previous chapters, the total local score in the SCT and the initial pronunciation score in the HRT were transformed into binary dummy-coded variables and relationships with clinical, demographic and comorbidity variables were analysed using point-biserial Pearson's correlation.

#### **6.6.3.1 *Demographic variables***

The association between cognitive variables and variables of age, years of education and estimate of intellectual ability were explored.

In the EDRec group, the level of intellectual ability as measured by NART was negatively associated with accuracy in the ROFT ( $r = .32, p = .05$ ) and positively related with correct pronunciation of the homographs in the Homograph Reading Test (HRT:  $r = .33, p = .04$ ). In terms of age, older people performed less well in accuracy recall in the ROFT ( $r = .30, p = .05$ ) and took longer to complete the designs in the segmented Block Design ( $r_s = .32, p = .04$ ).

### **6.6.3.2 Levels of co-morbid symptoms**

The relationship between neuropsychological performance and levels of anxiety, depressive and obsessive-compulsive symptoms was analysed.

Those with higher levels of obsessive-compulsive symptoms (OCI-R) scored lower in copy accuracy of the RCFT ( $r_s = .42, p < .01$ ).

### **6.6.3.3 Clinical variables**

Several clinical variables (duration of illness, age of onset, time from recovery, time spent in hospital, and BMI) were explored for potential association with neuropsychological performance.

In the EDRec group those who were recovered for a longer time spent more time copying the designs in the un-segmented Block Design trial ( $r_s = .44, p = .003$ ). Also, those who suffered from an eating disorder for longer performed better in the Sentence Completion Task ( $r = .34, p = .03$ ).

To examine potential confounder effects of demographic, co-morbid and clinical variables on differences between groups on neuropsychological performance, ANCOVAs were carried out and no effects were found.

### **A comparison between healthy controls and people with lifetime anorexia nervosa only**

In order to address the secondary hypothesis of this study, a between-groups comparison was carried out after excluding participants whose main lifetime diagnosis was BN.

Only a few differences in comparison with the profile seen in the whole group were found. These results were expected as 83% of the whole EDRec group had AN as main diagnosis.

The significant difference seen in the whole group in terms of order index in the ROFT fell to trend levels only. However, the difference on the HRT became significant ( $p < .05$ ) with an increased effect size of  $d = .47$ .

With regards to the additional cognitive aspects measured by ROFT (accuracy copy and recall, percentage of recall and organisational strategies),



differences were found only in accuracy (all  $p < .002$ ). These results replicate the outcomes from the comparison between the whole EDRec group and the HC group.

*Women with main lifetime diagnosis of anorexia nervosa in comparison with women with main lifetime diagnosis of bulimia nervosa*

With the objective of exploring potential differences in the cognitive profiles of participants with different main lifetime diagnosis (AN or BN), the EDRec group was separated into two groups: main lifetime diagnosis of AN ( $n = 35$ ) and main lifetime diagnosis of BN ( $n = 7$ ). In spite of the unequal sample sizes an exploratory analysis was carried out to highlight potential discrepancies between sub-groups. Only the results on the SCT showed differences between groups. The group who had anorexia as a main diagnosis obtained significantly higher scores in this task meaning that they took longer in doing verbal global processing (Mann-Whitney  $U = 0.65$ ,  $z = 2.02$ ,  $p < .05$ ,  $d = .65$ ). As the sample size in the group with past bulimia was very small, a further examination of the effect sizes was carried out. Effect size estimations revealed only moderate effect in one variable showing that the group with a predominant past diagnosis of AN made relatively more local completions in the SCT ( $d = .44$ ). All other effect sizes were small/negligible ( $d < .30$ ) suggesting little differences between the two groups.

Table 6.6 shows the comparison between the group recovered from AN and HC in the coherence variables. The results of the group with a main diagnosis of BN were added in the grey column as a point of reference but they were not included in the analyses presented in the table.

**Table 6.6 A comparison between those with main lifetime diagnosis of anorexia nervosa and healthy controls on neuropsychological indices of coherence**

	BN <i>n</i> = 7	AN <i>n</i> = 35	HC <i>n</i> = 42	Test statistic		<i>p</i> -value	Effect Size ( <i>d</i> )
				<i>t</i> -test	<i>MW</i>		
EFT medians <sup>b</sup>	7.5 (4.6-13)	6.6 (3.4-10)	12.2 (7.9-15.3)	n.a.	319.0	<.001 <sup>c</sup>	1.12
EFT errors <sup>b</sup>	0 (0-1)	0 (0-1)	1 (0-2)	n.a.	.466	.003 <sup>c</sup>	.72
EFT false claims <sup>b</sup>	1 (0-2)	1 (0-2)	2 (0-3)	n.a.	531.5	.03 <sup>d</sup>	.52
BD benefit from segmentation <sup>a</sup>	38.6% (15.0)	38% (15.2)	40.9 % (16.3)	.716	n.a.	.47	.18
RCFT order <sup>b</sup>	2 (1.8-2.8)	2.5 (2.2-2.7)	2.5 (2.2-3)	n.a.	647.0	.36	.20
style <sup>b</sup>	1.3 (0.9-1.8)	1.5 (1-1.8)	1.7 (1.5-1.8)	n.a.	460.5	.005 <sup>c</sup>	.70
coherence <sup>b</sup>	1.3 (1.1-.16)	1.5 (1.2-1.7)	1.6 (1.5-1.8)	n.a.	538.0	.04 <sup>d</sup>	.47
SCT local processing <sup>b</sup>	1 (0-1)	2 (1-3)	0 (0-1)	n.a.	291.5	<.001 <sup>c</sup>	1.32
HRT initial pronunciation <sup>b</sup>	15 (14-16)	15 (14-15)	15 (14-16)	n.a.	545.5	.04 <sup>d</sup>	.47

BN: main lifetime diagnosis of BN; AN: main lifetime diagnosis of AN; HC: healthy controls

<sup>a</sup> *t*-test = test statistics for *t*-test pairwise comparisons for data normally distributed, mean values displayed with standard deviations.

<sup>b</sup> *MW* = test statistics for Mann-Whitney *U* for data not normally distributed, median values displayed with upper and lower quartiles.

<sup>c</sup> = Results that remained significant ( $p < .05$ ) after Hochberg correction for multiple testing (Hochberg, 1988). <sup>d</sup> = Results dropped to non significant levels ( $p = .12$ ).

*A comparison between people with a lifetime restricting anorexia and bulimic syndromes (binge purging anorexia nervosa, purging anorexia nervosa and bulimia)*

In an endeavour to examine potential discrepancies in the cognitive profiles according to main ED symptoms an exploratory analysis was conducted after subgrouping the EDRec group into restricting ( $n = 14$ ) and binge/purge ( $n = 28$ ) syndrome categories: those who had restrictive symptoms only had a lower coherence index ( $d = .58$ ) and obtained lower scores in recall accuracy ( $d = .56$ ).

In summary, several analyses between sub-groups of the recovered sample according to their main lifetime diagnosis and the HC group were carried out. The results in terms of cognitive profile, after excluding those with a main lifetime diagnosis of BN, did not significantly differ from the results of the comparisons between the whole EDRec group and the HC group. After corrections for multiple testing, the only remaining difference was related to the general coherence index, which remained significant in the whole group comparison but not in the comparison with the main lifetime diagnosis of AN group. This result suggests that those with main lifetime diagnosis of BN had weaker coherence, particularly in order index, which decreased the general coherence index in the whole EDRec group.

## **6.7 Discussion**

The aim of this study was to examine the concept of central coherence in currently healthy people with a lifetime diagnosis of ED (EDRec).

The hypothesis, which was that women recovered from an ED would present a performance profile with enhanced detail processing and weak global coherence, was mainly confirmed by the results of this study. EDRec women performed extremely well in one of the tasks which benefit from enhanced detail function (the Embedded Figure Test). On the other hand, the recovered group displayed weaker performance in tasks which require a global strategy (Rey-Osterrieth Complex Figure, Sentence Completion Task, and – although less impaired – Homograph Reading Task). These results together raise the possibility that the hypothesis that weak coherence might be an endophenotypical trait for ED is correct as this

cognitive style is present independent of the illness state (Gottesman and Gould, 2003).

The subsidiary hypothesis was that the general cognitive profile of women with a main lifetime diagnosis of AN would differ from the profile displayed by those with a main lifetime diagnosis of BN. Therefore it was expected that a comparison between the HC group and the group with main lifetime diagnosis of AN would yield somewhat different results from those revealed by the comparison between the whole EDRec group and the HC group. This hypothesis was mainly rejected. Only a few differences were found between the whole EDRec group profile and the profile obtained by those with AN lifetime diagnosis only relative to the HC. Moreover, after correction for multiple testing the only remaining difference was that in the AN group the general coherence index did not reach levels of significance. One explanation could be the effects of the very few cases with a main lifetime diagnosis of BN on the whole EDRec group profile as mentioned above.

#### 6.7.1 Discussion of predictions

In accordance with the primary hypothesis of this study, most of the predictions based in the central coherence account were supported:

In the Embedded Figures Test (EFT) the EDRec group was found to be extremely fast in comparison with the HC group in identifying the hidden figures and made fewer errors and false claims. The latter difference disappeared after correction for multiple testing. Thus, the EDRec group was fast and displayed the error-free style also described in acute AN (see Chapter 4).

Their functioning in the Block Design Test (Un/seg BD), which is thought to benefit from piecemeal processing, was however, comparable to HC. It has been previously argued that the abilities required for a successful performance in the BD task involve a balance between analytical and integrative processing (Strauss et al., 2006). Analytical strategies are required to divide the whole into its constituent elements and integrative strategies are needed to re-create the whole from its parts. Similar abilities in solving the latter part of the task are required in tasks such as the Object Assembly wherein people with ED have demonstrated greater difficulties in relation to healthy control groups (see Chapter 2). This relative impairment might be attributable to weaker global processing. Therefore, it is expected that the EDRec

group would take longer in the un-segmented sub-test than in the segmented sub-test of BD since in the latter global abilities in creating the whole after segmentation are minimal. Thus, any possible advantage in spontaneously subdividing the designs might be obscured by the difficulties in re-creating the whole in the un-segmented sub-test of BD task. This explanation could account for the lack of difference between EDRec and HC groups in the benefit from segmentation yet does not clarify why in people with autism, who are also thought to have weak coherence, the effects of the required global strategies seem less prominent (Shah and Frith, 1993).

With regards to global visual processing abilities, the prediction that the EDRec group would display lower central coherence indices on the Rey Complex Figure Test (RCFT) relative to the HC was overall supported. All the indices of coherence were lower in this group, nevertheless, corrections for multiple testing revealed that order index did not differ between groups. This is an interesting finding as it indicates that the fragmentation in the drawing style (style index) was the predominant mechanism whereby groups differ rather than the attention to irrelevant details in the initial stage of the drawing (order index). Consequently, groups did not differ on the percentage of recall which was proved to be affected by the coherence of the drawing style in people with acute ED (see Chapters 4 and 5). On the other hand, these results show that the EDRec group might not be extremely impaired in global visual strategies.

The predictions made in relation to verbal coherence tasks were, in the main, supported. The EDRec group made more errors in the initial pronunciation of the homographs in the Homograph Reading Task but this difference failed to reach levels of statistical significance. Also, no differences were found on the effect of context position between groups. Once the sub-group with a main lifetime diagnosis of BN was excluded, the differences between the EDRec and the HC groups became significant in this task. These somewhat unclear results contrast with the straightforward conclusions from the Sentence Completion Task (SCT) in which groups clearly differed in terms of the difficulties in generating appropriate endings to the sentences. The functioning in the SCT is in line with the endophenotypical explorations in fathers of people with autistic spectrum disorders (Happé et al., 2001).

Finally, the prediction about the differences between groups in percentage of recall due to the effect of drawing style was not confirmed with the data from this

study as aforementioned. The EDRec group, although less accurate in the copy and recall trials of the RCFT, did not differ from the HC group in the percentage of memory loss. These results precluded a subsequent mediation analysis and replicate the results obtained in the studies of AN and BN in which drawing style measured by central coherence indices had an effect on percentage of recall. More interestingly, these results indicate some differences in the profile between acute and recovered samples, e.g. a bias towards details has a lower effect on general cognitive functioning perhaps due to better global strategies.

### 6.7.2 Exploring differences between women recovered from an ED and those in the acute phase of the disorder

This brief section addresses the discrepancies in the cognitive functioning between the group of recovered women (this study) and the groups described in the two previous chapters (AN and BN).

In general, the groups at normal weight (BN and EDRec) had an intermediate profile between those with acute AN and HC. The EDRec group was even more enhanced in detail processing than those with active AN (e.g. shorter times on the Embedded Figures Test) and also better than the BN group. In addition, the EDRec group displayed higher indices of visual coherence than those with acute AN. A similar performance was seen in those with acute BN. However, these observations with regards visual coherence were not statistically significant.

Overall the above evidence suggests that weight loss accentuates the difficulty in global integration and may weaken efficient detail processing.

Regarding other aspects of cognitive functioning measured by these tasks it was found that organisational strategy in the RCFT, which is thought to be linked to executive functioning, was similar to controls. This finding adds support to the proposed relative independence of central coherence from executive functions (Happé and Booth, 2008). The EDRec group had lower scores in accuracy in copy and recall trials of the RCFT than the HC group although both groups were comparable in terms of the memory component of the task (percentage of recall). It is uncertain why the recovered group had lower accuracy in the RCFT than both HC and those with acute AN. In this regard, people with BN again performed in a similar fashion as the recovered group. In the only study that has previously analysed the

performance of a recovered group in the RCFT, no differences were found between controls on recall accuracy (Pendleton Jones et al., 1991). In the case of BN, two previous studies found discrepant results. Murphy and collaborators (Murphy et al., 2002) found superior recall in a group with BN relative to a control group whereas Pendleton-Jones and colleagues found negligible differences between both (Pendleton Jones et al., 1991). Differences in intellectual abilities and age of the participants may explain these contradictory results.

Replication of this study may help to understand the low accuracy obtained by the EDRec on the RCFT. It is possible that the high detail focus may interfere with the task. However, the EDRec group as observed in the BN group obtained higher indices of coherence than the acute AN group therefore the bias towards details was less extreme than in AN. Finally, the lack of difference in percentage of recall between the EDRec and HC groups suggests that the loss of memory was not totally mediated by central coherence indices in the EDRec as seen in AN and in BN.

### 6.7.3 Previous findings in the study of recovered groups

Lately there has been a great increase of studies including recovered samples in the field of eating disorders with the main purpose of understanding and discovering aspects of potential vulnerability in ED development and maintenance.

Cross-sectional studies that have examined the basic neuropsychological performance of long-term recovered ED samples have demonstrated that other neuropsychological anomalies found in the active phase of AN are present after recovery whereas other studies suggest that certain functions are restored. For instance, aspects of set-shifting difficulties (Pendleton Jones *et al.*, 1991, Roberts *et al.*, 2007, Tchanturia *et al.*, 2004c, Tchanturia *et al.*, 2002), immediate memory and performance in Morse finger tapping task (Bosanac et al., 2007) seem to remain impaired in recovery. In terms of restored functions, Tchanturia and colleagues (Tchanturia *et al.*, 2007b) found no deficits in decision making in recovered women as opposed to those with acute AN. Also, decision making abilities have been described as a good predictor of weight recovery (Cavedini et al., 2006). Bosanac and colleagues (2007) found normal attention in women recovered from AN which suggest that the impaired aspects of attention seen in the acute state of the illness may result from the underweight state (Hamsher *et al.*, 1981, Kingston *et al.*, 1996,

Lauer *et al.*, 1999, Pendleton Jones *et al.*, 1991, Szmukler *et al.*, 1992). Finally, Pendleton Jones and colleagues (1991) did not find statistical differences between the performance of a recovered and a healthy control group on tasks measuring vigilance, memory, executive functions, verbal and visual-spatial abilities. However, an examination of effect sizes suggests that the recovered group performed poorer than healthy controls and similarly to those with active AN.

Brain studies have also shown anomalies in the functioning of recovered women such as altered insula response to taste stimuli (Wagner *et al.*, 2008), abnormal brain activation in reward processing (Frank *et al.*, 2006, Wagner *et al.*, 2007) and in response to food stimuli (Uher *et al.*, 2003), and anomalies in 5HT neuronal system activity (Frank *et al.*, 2002, Kaye *et al.*, 1991). In addition, Wagner (2006) also found structural abnormalities – cerebrospinal fluid volume and total and regional grey matter volume – described previously in recovered women (Katzman *et al.*, 1997, Lambe *et al.*, 1997) to be reversible after long-term recovery. Further studies would help to clarify these effects.

On the other hand, longitudinal studies have also shown conflicting evidence as to whether gain weight improves neuropsychological functioning (Southgate *et al.*, 2006). Although most of the studies show that weight gain reduces some of the impairments observed in underweight patients such as attention, problem solving and speed of cognitive processing (Kingston *et al.*, 1996, Lauer *et al.*, 1999, Moser *et al.*, 2003, Szmukler *et al.*, 1992), there is a number of functions that seem to remain impaired after weight gain such as aspects of set-shifting (Tchanturia *et al.*, 2002) and impairments in visual-spatial abilities, reaction time and immediate memory and recall (Gillberg *et al.*, 1996, Gillberg *et al.*, 2007, Green *et al.*, 1996, Hamsher *et al.*, 1981, Kingston *et al.*, 1996). Interestingly, Green and colleagues (Green *et al.*, 1996) and Tchanturia and colleagues (Tchanturia *et al.*, 2004c) found no correspondence between weight gain during treatment and improvements in neuropsychological performance.

Some of the tasks used in the present study were previously utilised in a study of a recovered population. Pendleton Jones and collaborators (1991) found that the recovered group was not impaired in recall accuracy on the RCFT, as opposed to the results of this study (Pendleton Jones *et al.*, 1991). The same study revealed no statistical differences in the EFT between HC and a weight recovered group although the latter performed poorer on the task ( $d = .80$ ). Again this result contradicts our



findings. Differences in administration of the task and clinical characteristics of the recruited samples may account for these conflicting results. Finally, using the original version of the Block Design task the recovered group performed like the control group with small effect sizes, similar to what we found in the present study.

Given that the evidence from studies looking at the cognitive functioning of fully recovered people with eating disorders is still limited and lacking of replication in most of cases, the reversibility status of impairments observed in the acute phase remains in the main uncertain. Similarly, replication of the present study would help to clarify which aspects of global and local processing may be affected by recovery or predict better outcomes. So far, it seems plausible that enhanced local processing will be a stable trait in ED, independent of the illness state. With regards to difficulties in global processing the available data suggest that although deficits are somewhat persisting these seem to be accentuated in the underweight state of AN. Also, taking into account the persisting deficits found in set-shifting abilities after recovery and the proposed possible interaction between executive functions and central coherence (Happé and Frith, 2006) it would be of interest to examine the relationship between these two aspects of cognitive functioning together. It could be hypothesised that performance on some of the tasks presented here is mediated by set-shifting difficulties and that the interaction between these two aspects of cognitive functioning would predict recovery to some degree.

#### 6.7.4 Possible confounders

The EDRec group had higher levels of co-morbid symptoms of anxiety, obsessive-compulsive and depression relative to the HC group. Persisting co-morbidity has been commonly described in recovered samples (Holtkamp *et al.*, 2005, Srinivasagam *et al.*, 1995, von Ranson *et al.*, 1999, Wagner *et al.*, 2006a).

Importantly, indices of weak coherence (strengths in detail processing and weak integration) were not associated with symptom levels of co-morbid conditions (symptoms) in the EDRec group. In acute illness cases, anxiety was associated with measures of coherence in BN (see Chapter 5). The results presented here suggest that weak coherence is therefore relatively independent from transitory co-morbid conditions.

Severity of the illness as indicated by the length of it was minimally associated with performance on the Sentence Completion Task and positively associated with outcome in exploratory analyses and. In the main, illness duration seems irrelevant to cognitive performance.

The EDRec group had a lower mean BMI than the HC group. The main part of this group had previously had AN and it is known that women recovered from AN tend to have lower BMI than the normal population (Hebebrand et al., 1996) and low body fat composition (Frey et al., 2000). However, BMI was not related to any coherence variable in the EDRec group which gives support to the hypothesis that weak coherence is independent of nutritional status.

#### 6.7.5 Limitations of the study

This study has several limitations. Firstly, the definition of recovery used here is based mainly on weight and behaviour related criteria which have been considered as first signs of recovery but do not take into account other relevant aspects of the psychological recovery in ED such as attitudes and obsession related to food, shape and weight which may remain unobservable. However, inclusion criteria relative to the time required to be free of behavioural symptomatology may have decreased the possibility of including participants in partial remission (Kordy et al., 2002). Secondly, the cross sectional design used here is somewhat unsatisfactory in that it is questionable whether those who are able to achieve recovery are representative of the eating disorder population as a whole or whether they are an atypical subgroup, possibly less severe, of the eating disordered population. This however would err on the side of reducing any trait effect. Nevertheless, the methodology that involves inclusion of a recovered group has been widely employed in the eating disorder literature to examine for trait versus state markers (Bailer *et al.*, 2007, Wagner *et al.*, 2008, Wagner *et al.*, 2007) and has produced some interesting findings (see section 6.7.3). Longitudinal studies would add to the interpretation of these studies. Thirdly, although it was not part of the primary hypothesis of this study, it would have been interesting to formally explore the differences between women with main lifetime diagnosis of AN and BN in terms of cognitive profiles. The small sample size of the latter group precluded any definitive inferences on the possible difference or similitude in the cognitive profile of these two sub-groups.

Finally, ceiling effects (both the EDRec and HC group performed well on the task with little score variance) were observed in the Homograph Reading Task which might preclude the possibility of finding differences between the recovered and control groups.

#### 6.7.6 Strengths of the study

Some strengths of this study are noteworthy. Firstly, this is a relatively large study in women recovered from an eating disorder. Forty-two participants have been assessed on neuropsychological functioning which exceeds the sample size previously used in most of the studies of this nature. Secondly, this is the first study in recovered women looking specifically at aspects of local and global information processing. Only one study has utilised some of the tasks described here with a focus on the general cognitive functioning in full-recovered participants (Pendleton Jones *et al.*, 1991) and one study used the original version of Block Design in a sample of mixed (different stages of recovery) AN (Gillberg *et al.*, 2007). Finally, all participants were free of medication which eliminates the effect of this potential confounder on cognitive functioning.

#### 6.7.7 Clinical and research relevance of the findings

Women recovered from an ED have shown a cognitive profile characterised by an enhanced detail processing and relative difficulties in global processing (weak coherence) as seen in acute phases of the illness. These findings may have implications for clinical practice and future research.

Traits that persist after recovery suggest that they were present premorbidly and might configure factors of vulnerability to the disorder (Anderluh *et al.*, 2003, Kordy *et al.*, 2002). It is possible to propose that weak coherence may trigger core behavioural and cognitive traits of ED such as perfectionism, fear of mistakes and change, and make them enduring even after recovery (Holtkamp *et al.*, 2005, Lilienfeld *et al.*, 2000, Matsunaga *et al.*, 2000, Srinivasagam *et al.*, 1995).

Also, examining the subtle differences in the neuropsychological profile between current and recovered participants would shed light on what elements might be helpful to address in treatment. The EDRec group in this study maintained an extremely efficient detail processing but the difficulties in global processing were

less extreme than in acute AN. Therefore, it might be arguable that increasing global processing skills would aid recovery. As mentioned in previous chapters, integrating these observations into a treatment approach that encompasses motivationally enhanced neuropsychological feedback (Lopez *et al.*, 2008a, Treasure *et al.*, 2007a) or cognitive remediation therapy (CRT) to enhance global processing strategies (Baldock and Tchanturia, 2007, Tchanturia *et al.*, 2007a, Tchanturia *et al.*, 2008) may improve metacognitive skills and moderate the bias towards detailed processing of information in currently ill women. This type of training might help to accelerate the recovery process making patients more cognitively able and receptive to traditional psychological therapies. However, the effect of this kind of pre-therapy intervention on subsequent treatment and outcome has not been fully examined yet. It is extremely important to test the association between cognitive abilities/deficits and behavioural ED symptoms in order to better understand how weak coherence is expressed in daily life activities, behaviours, and other aspects of the ED.

Furthermore, there is a need to further explore how persisting cognitive anomalies interact with recovery and relapse. For example, as recovered people have also been shown to have difficulties with set-shifting (Roberts *et al.*, 2007, Tchanturia *et al.*, 2004c) it is possible that the interactive combination of weak central coherence and difficulties in set-shifting may make recovery more difficult. In addition brain imaging studies would help to explore neurobiological pathways responsible for weak coherence and recovery in ED.

In a wider context, this study adds to the evidence supporting a common endophenotype between autism spectrum disorders and ED. Also, these findings give empirical endorsement to the suggestion that ED form a diagnostic cluster in association with obsessive-compulsive disorders (Hollander *et al.*, 2007) since individuals with the latter have also been found to have a bias towards detail processing of information in neuropsychological testing as do women with anorexia nervosa (Savage *et al.*, 1999, Sherman *et al.*, 2006). Obsessive-compulsive personality traits were found to contribute to poor global processing in ED (Tokley and Kemps, 2007). In autism spectrum disorders weak coherence is a potential endophenotype as several studies have found that the first-degree relatives are better in tasks that require a detail strategy (Baron-Cohen and Hammer, 1997, Baron-Cohen *et al.*, 2006, Bölte and Poustka, 2006, Happé *et al.*, 2001). Difficulties in global processing were also evident in parents, particularly fathers of people with ASD, as

measured by the Sentence Completion Test (Happé et al., 2001), who displayed similar performance to the EDRec group in this study. Collaborative research work with specialist teams in ASD and OCD would help to clarify this hypothesis.

As a final point, the results of this study support the potential trait hypothesis of weak coherence in ED, as opposed to a state, since this characteristic was present in recovered people. This observation fulfils another criterion in the exploration of weak coherence as an endophenotype for ED. Research into pairs of affected and unaffected family members of people with ED and studies on genetics are needed to explore the endophenotype hypothesis further.

## **6.8 Conclusion**

The aim of this study was to examine whether women recovered from an eating disorder (ED) would also show weak coherence and thus, explore the criterion of state independency for an endophenotype in psychiatry (Gottesman and Gould, 2003, Gould and Gottesman, 2006).

The recovered ED group showed a cognitive profile consistent with the weak central coherence hypothesis with an extremely good detail processing and difficulties in global processing. Only small differences were found on the profiles of those whose main lifetime diagnosis was AN versus BN.

The finding that weak coherence is a stable characteristic rather than a state effect suggests that it may be an endophenotype for ED and as such it is independent of illness state.

## **7 FROM THE DETAILS TO THE ‘BIGGER PICTURE’**

### **7.1 Introduction to the chapter**

This chapter endeavours to summarise the findings described in Chapters 4 through 6 with the final objective of providing a ‘bigger picture’ of the weak central coherence account in ED. A detailed exploration of how the weak central coherence trait is distributed in the healthy and eating disorder population and of how these groups varied in the expression of the trait is described. The second objective is to explore whether indices of weak central coherence generate a unitary concept and whether this concept relates to autistic-type traits. Finally, by providing a comprehensive analysis of the results, this chapter aims to contribute to a better understanding of the concept of weak central coherence in general.

In order to reach the aforementioned aims, the chapter is divided into a series of small studies that contribute to the final ‘bigger picture’. Firstly, all the four groups that took part in this project are compared across tasks measuring central coherence. Secondly, an exploration of individual differences in test performance with a closer examination of those who scored at ‘the extremes’ is described to assist in answering the question of *who* has weak central coherence. Thirdly, to explore whether central coherence is a single, underlying concept expressed in the central coherence battery, the results of a factor analysis are presented and explored in both the ED and HC samples. Finally, an examination of the potential relationship between autistic-type traits and weak central coherence indices is provided.

### **7.2 Summarising the findings**

#### **7.2.1 An examination of the four groups**

The purpose of this section was to summarise and compare findings on central coherence across the four groups that took part in this study. Therefore, results from performance in central coherence tasks of AN, BN, EDRec and HC groups were entered in between-group analyses. Also, a brief comparison between

ED groups (including AN, BN and EDRec<sup>9</sup>) is provided. In Chapters 4 through 6, it was demonstrated that all the ED groups differed from the HC group in most of the examined variables of central coherence, and especially in the visual-spatial domain. It was expected that no major differences in the central coherence profile would be found between ED groups.

### **7.2.1.1 Data analysis**

The same variables used to examine central coherence in the previous chapters were analysed: benefit from segmentation in the Un/Segmented BD task; detection time and false claims in the EFT; order, style and central coherence indices of RCFT; response latency and number of local completions in the SCT; and number of errors in the initial pronunciation of HRT. Differences between groups were also explored in accuracy and organisational strategies in the RCFT. Finally, the influence of some demographic and clinical variables on task performance was also analysed.

Analyses were carried out in SPSS version 16. A one-way between-groups ANOVA with Tukey HSD post-hoc test was used for normally distributed data. Its non-parametric alternative, Kruskal Wallis test, was used otherwise. Normality of the data distribution was assessed according Shapiro-Wilk test for normality confirmed by the visual inspection of plots per group in each variable.

Most of the variables were non-normally distributed in at least one group (even after attempts of transformation) except for accuracy copy and recall and percentage of recall of the RCFT, benefit from segmentation of the BD test, anxiety, intellectual ability and BMI.

### **7.2.1.2 Results**

All four groups were equivalent in terms of age (Kruskall Wallis test:  $\chi^2 = .32$ ,  $df = 3$ ,  $p = .96$ ) and intellectual ability ( $F_{(3,167)} = .64$ ,  $p = .59$ ). All ED groups had higher levels of anxiety ( $F_{(3,167)} = 35.89$ ,  $p < .001$ ; AN>BN=EDRec>HC), depression (Kruskall Wallis test:  $\chi^2 = 68.81$ ,  $df = 3$ ,  $p < .001$ ; AN=EDRec>BN> HC) and OCD symptoms (Kruskall Wallis test:  $\chi^2 = 48.45$ ,  $df = 3$ ,  $p < .001$ ; AN> B =

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<sup>9</sup> ED groups will refer to those with current or past eating disorders i.e. AN, BN and EDRec groups.

EDRec > HC), relative to the HC group. The group with AN had the lowest BMI ( $F_{(3,167)} = 68.59$   $p < .001$ ; HC=BN=EDRec>AN).

Results from neuropsychological assessments of central coherence revealed that groups differed in most of the variables assessed. Table 7.1 shows details of the results which can be summarised as follows:

a) Tasks that benefit from local processing skills: As seen in the table, groups with a history (past or present) of ED were generally faster and more accurate than the HC in the EFT. In the Un/Segmented BD, the group with BN and EDRec equally benefited from segmentation but to a lesser degree than HC and AN demonstrating their better local processing skills.

b) Tasks that benefit from global processing skills: In the visual processing task of RCFT, indices of coherence were higher in the HC group than in the ED groups indicating superior global processing in the former group. The scenario was more complex in verbal tasks. In the SCT, no differences were found in the number of local completions and it was a rare event among all groups. However, the fact that the HC was faster in giving an appropriate, global ending to the sentences suggests that this group has better global processing skills in the verbal domain. In the HRT, HC and AN made fewer errors than the BN and EDRec groups.

**Table 7.1 Central coherence variables across groups**

Test	Variable	$\chi^2$	$F_{(3,167)}$	$p$	
EFT	False claims	16.81	n.a.	.001	HC>BN>AN=EDRec
	Time	19.44	n.a.	<.001	HC>AN>BN>EDRec
BD	Benefit segmentation	n.a.	1.38	<.001	HC=AN>BN=EDRec
RCFT	Order	13.45	n.a.	.004	HC>EDRec>BN>AN
	Style	12.28	n.a.	.006	HC>BN>EDRec>AN
	Central Coherence	15.85	n.a.	.001	HC>BN=EDRec>AN
SCT	Local completions	3.765	n.a.	.288	No differences
	Response latency	25.41	n.a.	<.001	HC<AN<EDRec=BN
HRT	Errors initial pronunciation	6.54	n.a.	.088	HC=AN<BN=EDRec

n.a. = not applicable



Further analysis of the neuropsychological performance obtained from the analysis of the RCFT showed that groups also differed in scores on organisational strategies (Kruskall Wallis test:  $\chi^2 = 8.91$ ,  $df = 3$ ,  $p = .03$ ; HC>BN=EDRec>AN), accuracy copy ( $F_{(3,167)} = 29.95$ ,  $p < .001$ ; HC=AN>EDRec=BN), accuracy recall ( $F_{(3,167)} = 7.41$ ,  $p < .001$ ; HC>AN>BN=EDRec), and percentage of recall ( $F_{(3,167)} = 2.83$ ,  $p = .04$ ; HC=BN=EDRec>AN).

When only the three ED groups were analysed, statistical differences were found only in the number of false claims in the EFT (Kruskal Wallis test:  $\chi^2 = 15.10$ ,  $df = 2$ ,  $p = .001$ ). Visual inspection of mean ranks showed that the group with BN made more false claims than those with AN and the EDRec. A difference that reached a statistical trend of significance was found in the median time of searching for the embedded figures in the EFT (Kruskal Wallis test:  $\chi^2 = 5.00$ ,  $df = 2$ ,  $p = .08$ ) where the AN group took longer than the BN group and EDRec. EDRec was the fastest among the ED groups.

Other variables resulting from the analysis of the RCFT were explored. A one-way between-groups ANOVA showed a statistically significant difference in the scores for accuracy in the copy trial of the test. The actual difference in mean scores was moderate as shown by an eta squared effect size of 0.34. Post-hoc comparison using the Tukey HSD test indicated that the mean score for the AN group was significantly different from the BN (mean difference = 4.5, std. error = .69,  $p < .001$ ) and the EDRec group (mean difference = 5.4, std. error = .69,  $p < .001$ ). The BN group did not differ significantly from the EDRec group (mean difference = .52, std. error = .69,  $p = .73$ ).

### **7.2.1.3 Conclusion**

In sum, on indices of visual-spatial global processing the ED groups showed poorer performance but were relatively superior in local processing than HC. In verbal coherence HC did better than ED groups in the SCT and HRT although in the latter task AN did not differ from HC.

All the results from this section confirmed the hypotheses and as discussed in Chapters 4 through 6 they give support to the weak coherence hypothesis in ED. However, they highlight small differences that occur between ED groups that could

be informative of variations within the endophenotype. For example, the fact that the group with AN obtained the lowest coherence indices in the RCFT together with low percentage of recall (visual memory), indicates that this group is the most impaired in global visual processing among the ED groups. However, they are the least impaired in verbal coherence. Also, the BN and EDRec groups were the fastest in local processing but whereas the cost for BN was accuracy, this was not seen to be compromised in the EDRec group.

### **7.3 Extreme Performance Across Groups**

So far, it has been proven that ED groups show a cognitive profile in line with the weak central coherence theory. However, differences at the individual level may occur within groups. This section was aimed at exploring those differences within groups in the performance of tasks of central coherence. Firstly, in order to reduce the variance within groups, analyses were carried out to identify the proportion of individuals that obtained ‘extreme’ scores on central coherence tasks. This procedure revealed which central coherence variables showed the highest sensitivity to discriminate between good and poor performance. Secondly, based on the previous analyses the question of who has weak central coherence was addressed.

#### **7.3.1 ‘Extreme’ performance in the central coherence tasks**

Happé and Frith (2006) have proposed that the concept of weak central coherence may vary across the general population. Individual and group variations are expected in that all the four quadrants of the proposed two-dimension concept of weak central coherence (see Figure 1.2) would be filled. Thus, some people would be good at local and global processing, some would be good at local and poor at global processing and vice versa, and others would be poor at both.

From the data described in the previous section, it is relatively clear that those women with current or past history of ED have, in general, weak central coherence. However, as mentioned before, ED groups tend to differ in terms of levels of performance in comparison with the HC group across tasks. Also, from the variance of the results of the studies presented in Chapters 4 through 6 we know that not all

individuals within a group display the trait in the same manner and that some of them may not display the trait at all.

This section has the purpose of revising the data distribution of the four groups to identify the proportion of individuals within groups that score at the extremes in every task indicating either difficulties in global processing or superior local processing relative to the scores of the HC group. It is hoped that this procedure will provide a bigger picture as to how the central coherence concept is distributed in the ED population.

### ***7.3.1.1 Data Analysis***

The procedure to extract the proportion of individuals in each group with ‘extreme’ scores in each variable of central coherence involved a transformation of individual data into a binary dummy variable (0-1) to identify cases that scored below the 25<sup>th</sup> percentile (Q25)/above the 75<sup>th</sup> percentile (Q75) or  $\pm 1SD$  away from the mean of the scores obtained by the healthy control group. The decision over which percentile was selected or whether the use of 1SD was appropriate was made according to the distribution of the data and the direction of the scoring of each variable so that extreme scores reflect either better local processing or poorer global processing (weak central coherence). For example, for non-normally distributed data percentiles were used and SD was used otherwise; below Q25 was used for tasks in which higher scores reflect better global processing (those below Q25 would be more impaired in global processing); over Q75 was used for variables in which higher scores reflect better local processing.

The proportions of individuals scoring at extremes on the central coherence variables were compared between groups using Pearson chi square test ( $\chi^2$ ). A logistic regression analysis was carried out to test whether levels of co-morbid symptoms (anxiety, depression and obsessive-compulsive symptoms) predicted extreme scores in variables where group differences were significant. The dependent variable corresponded to the cases coded as showing ‘extreme’ (1) and ‘no extreme’ scores (0). Co-morbid levels of symptoms were entered as covariates predictors in the model using the ‘enter’ method. Assumptions of multicollinearity (inter-correlations among predictors should be lower than  $r = .9$ ) and singularity (none of

the independent variables were a combination of other independent variables) of the independent variables were met.

### **7.3.1.2 Results**

The proportion of individuals per group presenting extreme scores per tasks is shown in Table 7.2 along with the results of chi square tests. All the significant results in the table remained significant after correction for multiple testing ( $p < .05$ ). Figure 7.1 is a graphic display of these results.

Analyses revealed that extreme scores across tasks are over-represented among those with current or past ED in comparison with the HC group. Thus, more extreme scores were found in ED groups on variables such as speed and time in the EFT indicating strong local processing and in central coherence indices in the RCFT, response latencies in the SCT and errors in the initial pronunciation of the homographs in the HRT, indicating difficulties in the spontaneous use of global strategies. One can conclude from these results that on those variables where significant results were found between groups were most sensitive in detecting weak central coherence biases.

A logistic regression analysis revealed that the level of co-morbid symptoms predicted a marginal proportion of extreme scores found in the central coherence index on RCFT only ( $\chi^2 = 14.42, df = 3, p = .002$ ). The total of the variance predicted by a model including anxiety, depression and obsessive-compulsive symptoms was estimated between 8.5 and 11.3% and none of the mentioned co-morbid variables contributed significantly to the model (all  $p > .25$ ).

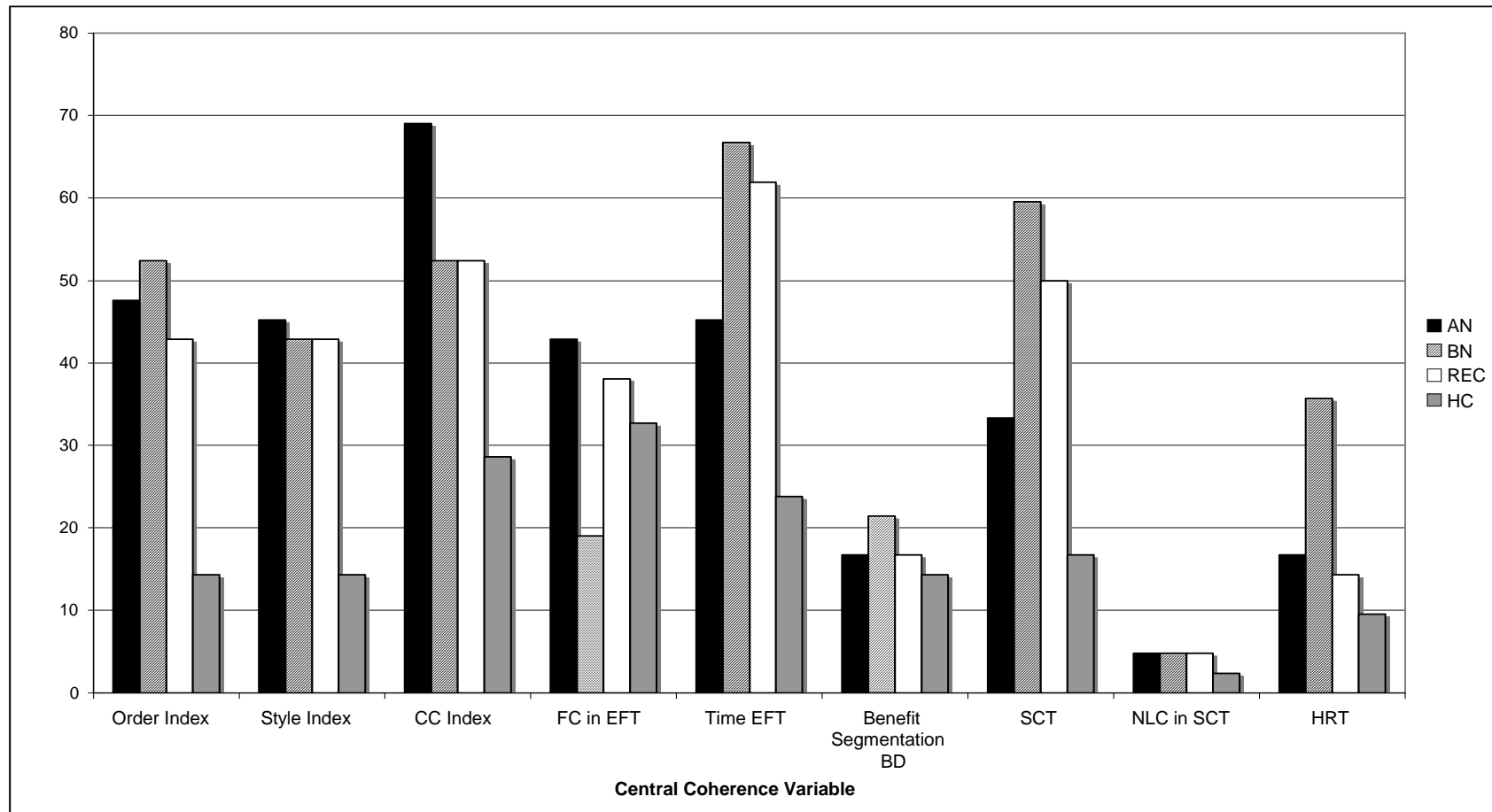
**Table 7.2 Between-groups comparison of individuals per group with ‘extreme’ scores per task**

Test	Variable	AN	BN	EDRec	HC	Pearson $\chi^2$ df (3)	<i>p</i>
EFT	Low false claims (accuracy)	42.9	19.0	38.1	32.7	6.13	.105
	Good speed (Time)	45.2	66.7	61.9	23.8	18.93	<.001
BD	Low benefit from segmentation	16.7	21.4	16.7	14.3	.792	.851
RCFT	Low order index	47.6	52.4	42.9	14.3	15.4	.001
	Low style index	45.2	42.9	42.9	14.3	11.8	.008
	Low central coherence	69	52.4	52.4	28.6	13.98	.003
SCT	High local completions	4.8	4.8	4.8	2.4	.447	.930
	High response latency	33.3	59.5	50	16.7	18.74	<.001
HRT	High errors initial pronunciation	16.7	35.7	14.3	9.5	10.81	.013

### 7.3.1.3 Conclusions

From the analyses carried out in this section it is possible to conclude that extreme scores indicative of both strong local processing and weak global processing were over-represented in women with current or past ED in comparison with the HC group. Secondly, extreme scores in central coherence tasks are relatively independent from the co-morbid conditions associated with ED. Finally, there is a proportion of individuals in the ED group that do not show extreme scores in the coherence tasks.

**Figure 7.1 Percentage of individuals per group with 'extreme' scores per task**



Order Index: Extreme low index; Style Index: Extreme low index; CC Index: Extreme low central coherence index; FC in EFT: extreme low number of false claims (accuracy); Time EFT: Extreme speed time in EFT; Benefit Segmentation BD: Extreme low benefit from segmentation; SCT: extreme high local score; NLC in SCT: Extreme high number of local completions; HRT: extreme high number or errors in the initial pronunciation in HRT.

### 7.3.2 Who has weak central coherence in the ED population?

The results from the previous section suggested that ‘extreme’ scores in central coherence vary across groups and measures, and that there is an important proportion of participants in the ED group that do not show impairments in tasks that benefit from global skills, superiority in tasks that benefit from local processing or both.

Therefore, although the ED groups showed the greatest proportion of individuals scoring at extremes in central coherence variables, it is expected that an analysis of individual performance profiles across tasks may give a more accurate picture about who in the ED and HC groups meets the two criteria required to be ‘a case’ of weak central coherence, i.e. present both a superior local processing and weaknesses in global processing.

The purpose of this section was to identify such cases and compare the four groups in terms of the proportion of individuals that may have weak central coherence. It was expected that in all groups some women fulfilled the criteria for weak central coherence but that that proportion would be significantly lower in the HC group in comparison with the ED groups.

#### 7.3.2.1 *Data Analysis*

The already transformed data that indicated individual extreme performance in each variable were used to create two groups: ‘cases’ and ‘non cases’ of weak central coherence. In order to do so, an extra variable (‘WCC case’: case of weak central coherence) was created with the individuals that have **at least one** extreme score on tasks showing **superior local processing** (low benefit from segmentation in the un/segmented BD test, low false claims (more accuracy) and shorter detection time in the EFT) **AND at least one** extreme score on tasks showing **difficulties in global processing** (low central coherence index in the RCFT, low number of local completions in the SCT, shorter response latency in the SCT, low errors in the initial pronunciation in the HRT). Frequency analyses were carried out per group and proportions between groups were compared with Pearson chi square.

### 7.3.2.2 Results

The comparison of proportions of women fulfilling both criteria for weak central coherence per group is shown in Table 7.3.

**Table 7.3 Between-groups comparison of individuals for each group fulfilling criteria for ‘weak central coherence’**

	AN	BN	EDRec	HC	Pearson $\chi^2$ df (3)	<i>p</i>
% weak central coherence cases	<b>47.6</b>	<b>66.7</b>	<b>54.8</b>	<b>16.7</b>	23.07	<b>&lt;.001</b>
% of non cases	52.4	33.3	45.2	83.3	18.93	

As expected, all the ED groups exceeded significantly the proportion of individuals showing weak central coherence relative to the HC group (all  $p < .05$ ). Interestingly, the BN group showed the highest proportion of individuals with weak central coherence among the ED groups but this difference was not significant (Pearson  $\chi^2 = 3.16$ ,  $df = 2$ ,  $p = .206$ ).

### 7.3.2.3 Conclusion

The overall conclusion of this section is that the groups of women with current or past ED present a higher proportion of cases that can be identified as having ‘weak central coherence’ relative to the HC group. There is still around a half of individuals belonging to the ED groups that do not present weak central coherence or that may display one but not two of the criteria. The existence of such variability of weak central coherence within ED groups, in addition to the fact that proportions of individuals with weak central coherence across ED diagnosis differ, may reflect the heterogeneity of this population as discussed in Chapter 1.



## 7.4 Is Central Coherence a Unitary Concept?

In the previous sections we have addressed some aspects related to how the concept of weak central coherence is distributed across individuals who suffer or have suffered from an ED in comparison with a group who have never had an ED. It was demonstrated that (1) part but not all of the ED participants presented the cognitive style of weak central coherence, (2) weak central coherence was present across ED diagnosis and ED status (active versus recovered), and (3) the probability of presenting weak central coherence in those with current or past ED was two or three fold higher than in HC women.

Another interesting aspect with regards to the central coherence account is the question of whether this is a unitary, single concept measured by tasks that uncover a common underlying mechanism and would, therefore, be a characteristic that rules the overall cognitive functioning in an individual as originally suggested by Frith (Frith, 1989). Two elements could be considered here. Firstly, the question as to whether central coherence involves a single concept that manifests in a continuum from strong local to strong global processing (central coherence within domain) is still of relevance, at least in the unexplored field of ED. Secondly, the question of whether measures tapping different domains of coherence (e.g. verbal and visual) express a single underlying mechanism expressed in a general predominant cognitive style (central coherence across domains) needs to be addressed.

The literature in the field of ASD suggests that there are two aspects of information processing, global and detail-focused processing, which are somewhat independent, challenging the hypothesis of a continuum in the trade-off between local and global processing. This observation would be true particularly in typical developing children and young adults without the disorder (Booth, 2006, Happé and Frith, 2006). This two-dimensional concept (global and local processing) has been used throughout the present thesis. A continuous concept, however, would still be useful in respect to the ASD population where local and global processing are generally seen to have a trade-off relationship (Booth, 2006, Teunisse *et al.*, 2001).

In the previous section it was shown that around a half of those with ED would fall in the good local/poor global quadrant of the local versus global processing model suggesting that a continuous concept would also be appropriate in

the case of ED. However, the fact that the other half of the ED sample did not show this profile suggests that they should be distributed in the other quadrants with variations in the relationship between local and global processing abilities. Therefore, it is highly possible that some individuals exhibit profiles where local and global processing are positively associated giving support to the two-dimensional instead of continuous concept of central coherence.

In terms of the unitarity of central coherence across domains, studies in ASD are inconclusive and conflicting results have been found (Booth, 2006, Burnette *et al.*, 2005, Teunisse *et al.*, 2001).

Therefore, the objective of this section was to explore the unitarity of the concept of central coherence in ED by examining whether the tasks used to explore coherence in this study reflect a common underlying concept within and across modalities of processing (verbal/visual).

#### **7.4.1.1 Data Analysis**

The measures used in this thesis have been divided into those in which performance would benefit from local *or* global processing (see Chapter 3). Tasks that would benefit from local processing were Un/Segmented BD and the EFT. Tasks that would benefit from the use of global strategies were the RCFT, SCT and HRT. This division was made based on evidence from previous studies in the ASD population and theoretical underpinnings of the tasks.

To address the question of whether these tasks are tapping a common underlying mechanism of central coherence, the viability of carrying out an exploratory factor extraction, i.e. Principal Components Analysis (PCA) was assessed. The data explored were the key central coherence indices obtained per task considering the whole sample of participants of this study<sup>10</sup> ( $n = 168$ ): Benefit from segmentation of the BD, detection time of the EFT, central coherence indices (order and style) of the RCFT, response latency score of the SCT and number of errors in the initial pronunciation of the HRT.

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<sup>10</sup> A caveat to acknowledge in the present PCA is that the sample size of healthy controls was not sufficient to perform a factor analysis. Therefore ED groups' scores were included in the factors extraction and composite scores. It is expected that this procedure will have an effect on the data distribution on factor scores. Ideally, this PCA should be done with healthy control data only.

Sample size was adequate for such analysis. Kaiser-Meyer-Olkin's (KMO) test for measuring sampling adequacy and Bartlett's test of sphericity were conducted to assess factorability of the data. The KMO index indicates the proportion of common variance between variables and may reflect underlying factors. This index ranges from 0 to 1, reaching 1 when each variable is perfectly predicted without error by the other variables. Generally speaking, an index of .6 is suggested as the minimum value for a good factor analysis (Tabachnick and Fidell, 2001). The Bartlett test of sphericity indicates the presence of correlations among the variables that support the suitability of a factor analysis. The value of this test should be significant ( $p < .05$ ).

The PCA analysis was chosen over other methods of data extraction as the objective was to have an empirical summary of the data set (Tabachnick and Fidell, 2001) and to identify the underlying structure of the relationships between central coherence variables.

Composite scores per derived component were created adding standardised  $z$  scores of each relevant variable. To facilitate the construction of composite scores, all coherence indices were coded so that a positive score reflected strong global processing or strong local processing.

All analyses were carried out in SPSS Version 16.

#### **7.4.1.2 Results**

##### Principal Components Analysis

In general, low but significant correlations were found among some of the central coherence variables (see Table 7.4). Errors in the initial pronunciation did not correlate significantly with any of the other variables of coherence.

The six variables of central coherence were subjected to Principal Components Analysis (PCA). The factorability of the data was confirmed by Bartlett's test of sphericity (approx.  $\chi^2 = 142.1$ ,  $df = 15$ ,  $p < .001$ ). However, the KMO index was .54 indicating that the degree of common variance among the six variables was medium and not over the .6 suggested as the minimum recommended for a factor analysis. Therefore, it was expected that factors extracted would not account for a substantial amount of variance.

**Table 7.4 Correlation matrix of central coherence variables**

	U/S BD	EFT	HRT	SCT	Order RCFT	Style RCFT
U/S BD		.48**	-.09	-.18**	-.21**	-.21**
EFT			-.01	-.10	-.06	-.10
HRT				-.12~	.08	.08
SCT					-.05	-.04
Order RCFT						.534**

\*\*  $r_s p < .01$ , ~  $r_s p < .10$

Coherence indices: U/S BD= Benefit from segmentation in un/segmented Block Design Task; EFT= detection time in the Embedded Figures Test; HRT= number of errors in the initial pronunciation; SCT= total local score in the Sentences Completion Task; Order RCFT=Order index in the Rey-Osterrieth Complex Figure; Style RCFT= Style index in the Rey-Osterrieth Complex Figure

PCA revealed the presence of **three components** with eigenvalues exceeding 1 (Kaiser's criterion or eigenvalue rule), explaining 31%, 22.70% and 17.16% of the variance respectively. Using Catell's scree test (Catell, 1966), it was decided to retain these three factors. To aid in the interpretation of these three components Varimax rotation<sup>11</sup> was performed. The rotated solution confirmed the presence of three components that showed two strong loadings each. All variables loaded substantially on only one component. The three-component solution explained a total of 70.87 % of the variance in the data. All rotated factor loadings are presented in Table 7.5.

Components were named according to the characteristics of the tasks that grouped into factors. Thus, the first component that included style and order index of the RCFT only, was referred to as a **visual global processing**; the second component that grouped detection time of EFT and benefit from segmentation in BD was named **visual local processing**, and the third factor that grouped the two verbal tasks was called **verbal coherence** (both assessing ability to use verbal coherence skills). The fact that benefit from segmentation of the BD loaded negatively (although minimally) on the global processing component, suggests that this variable is in part related with global processing abilities as suggested in the discussion of Chapters 4 through 6.

<sup>11</sup> Oblimin rotation method was also used and yielded the same solution. Resulting components had low correlations with each other (correlation coefficients varied from -.03 to -.160) suggesting that the underlying factors are orthogonal.

**Table 7.5 Rotated components matrix with factor loadings (>.20) from the PCA of the six central coherence variables**

Central Coherence Variable	Components		
	Visual Global Processing	Visual Local Processing	Verbal Processing
U/S BD	-.211	.875	
EFT		.830	
HRT			.727
SCT			-.760
Order RCFT	.895		
Style RCFT	.895		

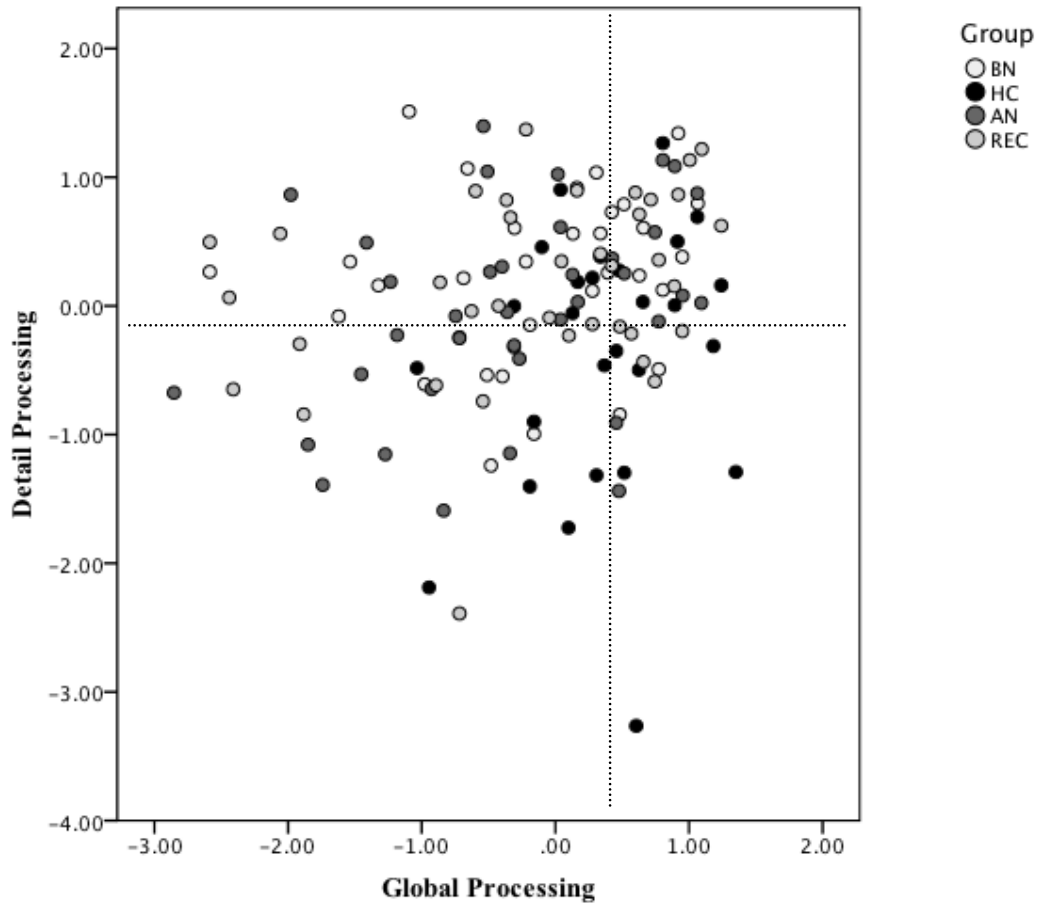
Composite scores per derived component were created adding standardised  $z$  scores of each relevant variable for each factor. Response latency score of SCT was recoded so that higher scores reflected better verbal global processing. Detection time in the EFT and percentage of benefit from segmentation in the BD were also recoded so that higher scores on that factor would suggest better local processing. Variables for verbal coherence factor did not need to be recoded. After all variables were prepared, composite scores per factor were obtained by averaging the respective standardised residual scores ( $z$ ).

Correlation analyses including ED and HC groups showed that global and local processing were low but positively correlated ( $r_s = .22, p = .004$ ), indicating that a good detail processing can go together with a good global processing and they do not necessarily represent a trade-off relationship. Verbal coherence was related to visual global processing on a trend level only ( $r_s = .14, p = .06$ ).

As an example of how global and detail processing may manifest in the population, we have displayed visual global and local processing in a scatter plot in Figure 7.2. This graph confirmed that individuals' scores spread out across the quadrants around the median scores of the HC group represented by a cross on the graph<sup>12</sup>. Differences between groups will be addressed later.

<sup>12</sup> The use of HC scores as a 'norm' was based on the assumption that they would represent the population without history of ED.

**Figure 7.2 Scatter plot showing individual distribution for local and global visual processing across groups**



When data were split into ED and HC groups, correlations were found between visual global and visual local processing in the ED group only ( $r_s = .306, p < .001$ ). These findings also suggest that good local processing was not necessarily achieved at the expense of weak global processing in ED groups.

#### Global, detail and verbal coherence factors

The four groups that took part in this study were compared according the scores obtained in each component derived from the PCA. As factor data within groups were non-normally distributed Kruskal-Wallis tests were used. Groups differed in all the three factors. Details of such comparisons are shown in Table 7.6.

Overall, these results support what has been described in the first section of this chapter when groups were compared across tasks. Interestingly, within the ED

group, the AN group seems to obtain somewhat different scores than BN and EDRec. The association between BMI (the variable that distinguished AN from BN and EDRec) with the three components was explored and found that in the ED groups BMI was positively correlated with visual local processing although this relationship was not statistically significant ( $r_s = .16, p = .06$ ).

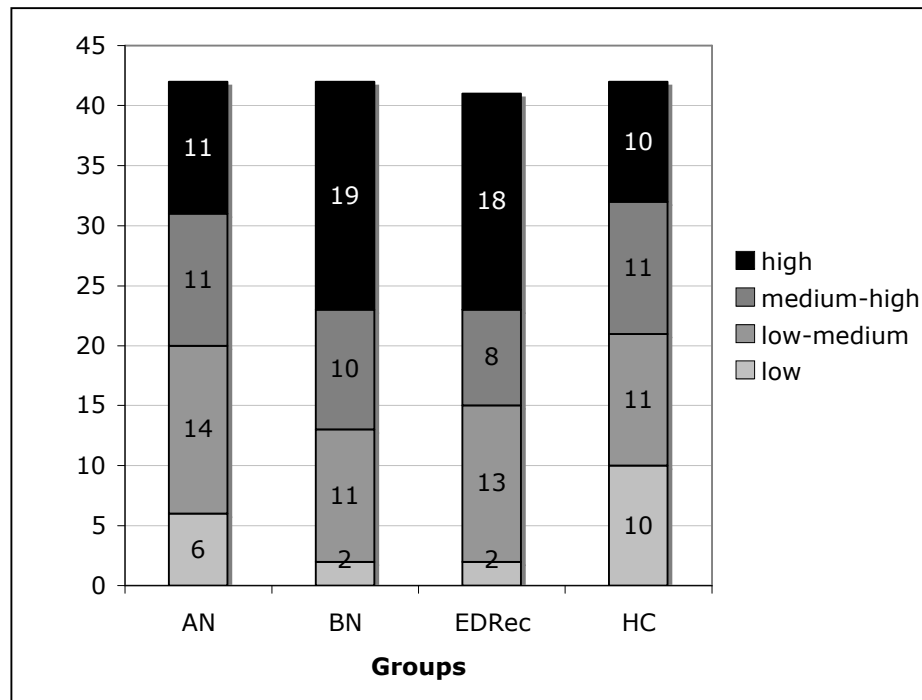
**Table 7.6 Central coherence factors across groups**

Component	AN	BN	EDRec	HC	$\chi^2$	$p$	Observations
Visual Local Processing	.05 (-.65-.51)	.30 (-.30-.75)	.29 (-.20-.76)	-.03 (-.94-.39)	9.5	.023	BN=EDRec>AN>HC
Visual Global Processing	-.29 (.86-.46)	.15 (-.55-.54)	.16 (-.60-.72)	.46 (.16-.89)	15.6	.001	HC>BN=EDRec>AN
Verbal Coherence	.26 (-.60-.62)	-.15 (-.61-.27)	.09 (-.65-.57)	.57 (.15-.92)	20.0	<.001	HC>AN>BN=EDRec

Data non-normally distributed therefore median and upper and lower quartiles are reported (Q25-Q75)

A comparison of the three factors across groups showed that individuals may not be distributed evenly across the four quadrants and that differences between groups exist. To explore this further, participants were then categorised into one of four subgroups for each component using as norms the scores obtained by the HC group. The four groups were: **low** performance if their mean score was below percentile 25<sup>th</sup>, **low-medium** if their mean score was between the 25<sup>th</sup> and 50<sup>th</sup> percentile, **medium-high** if their mean score was between the 50<sup>th</sup> and 75<sup>th</sup> percentile, and **high** performance if their mean score was between the 75<sup>th</sup> and 100<sup>th</sup> percentile.

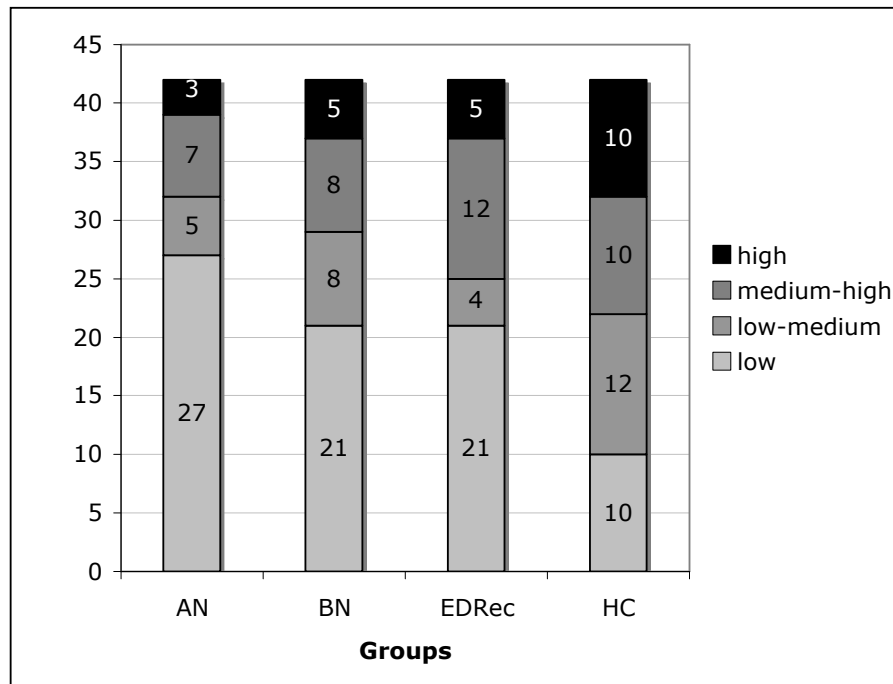
Participant characteristics for ED and HC groups categorised by this method in each factor are presented in the following graphs (Figures 7.3 to 7.5).



**Figure 7.3** Bar chart showing the frequency of participants per group categorised as presenting low, low-medium, medium-high, and high Detail processing

According to the above graph (Figure 7.3), it is possible to observe that the groups with a greater proportion of individuals scoring high in the detail factor are BN and EDRec. AN and HC follow a similar patterns of scoring although the HC have slightly more cases in the lower 50<sup>th</sup> percentile than the AN group. Despite the observable differences between groups, there were no statistically significant differences between the four groups (Pearson  $\chi^2 = 14.1$ ,  $df = 9$ ,  $p = .12$ ).

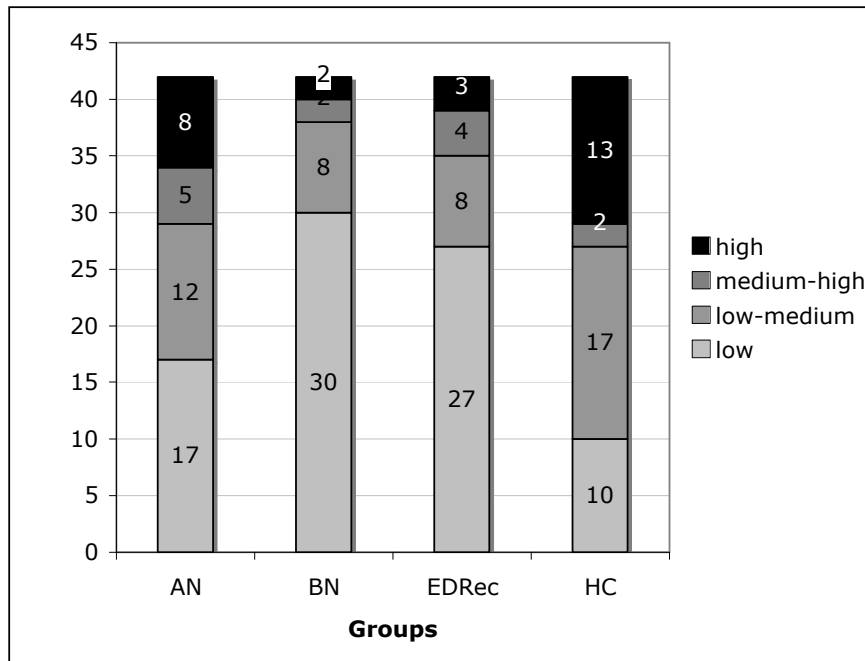




**Figure 7.4** Bar chart showing the frequency of participants per group categorised as presenting low, low-medium, medium-high, and high Global processing

This second graph (Figure 7.4) shows clear differences from the previous graph. Global processing abilities were much more impaired in ED groups than in the HC group ( $\chi^2 = 19.2, df = 9, p = .02$ ).

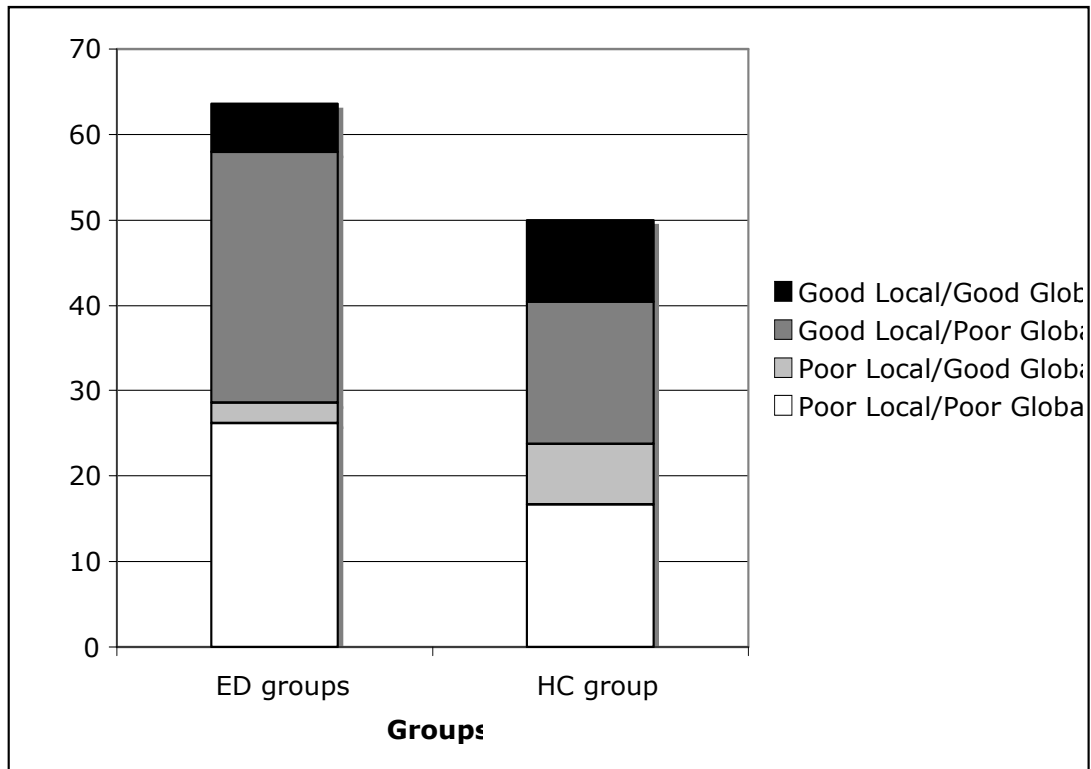
Finally, the graph below (Figure 7.5) displays a mixed scenario in the verbal coherence component. The BN and EDRec groups were the most impaired in verbal coherence abilities followed by the group of women with AN. The HC group had the greatest proportion of individuals scoring 'high' whereas the BN group the least, with only 2 women scoring over the percentile 75<sup>th</sup>. Pearson chi square test confirmed those differences between groups ( $\chi^2 = 30.08, df = 9, p < .001$ ).



**Figure 7.5** Bar chart showing the frequency of participants per group categorised as presenting low, low-medium, medium-high, and high Verbal Coherence processing

The question of who has weak central coherence was addressed again in light of the results of the PCA. Those with weak central coherence were defined as individuals who obtained scores below the 50<sup>th</sup> percentile in visual global processing and verbal coherence and above the 50<sup>th</sup> percentile in the detail processing.

There was a trend level of difference between those having weak central coherence in the ED groups versus the HC group with a third of the ED group ( $n = 37, 29.4\%$ ) and a sixth of HC ( $n = 7, 16.7\%$ ) fulfilling the criteria (Pearson  $\chi^2 = 2.65, df = 1, p < 0.9$ ). No differences were found between those having good local and good global processing (ED:  $n = 7, 5.6\%$  and HC:  $n = 4, 9.5\%$ , Pearson  $\chi^2 = .811, df = 1, p = .368$ ). Poor local and good global was found in three women in the HC group (7.1%) and one in the ED groups (2.4%) which reached significance ( $\chi^2 = 5.46, df = 1, p = .02$ ). The most impaired group (poor global and poor local) were found in seven HC (16.7%) and thirty three in the ED group (26.2%), results that were not significant ( $\chi^2 = 1.57, df = 1, p = .21$ ). These results are graphically displayed in Figure 7.6.



**Figure 7.6** Bar chart showing the proportions of participants per group categorised according to combinations of good/poor local and good/poor global scores

### 7.4.1.3 Conclusions

This section addressed the question of whether the measures in the central coherence battery used in this study were able to tap a common underlying mechanism of coherence. In order to reach that objective, a Principal Component Analysis (PCA) was performed. This analysis allowed for the exploration of the concept of central coherence across and within groups. Three components were extracted from this analysis: Visual local processing, visual global processing and verbal coherence.

The trade-off relationship suggested in the previous section of this chapter, at least for the ED group as a result of individual-task analysis, was challenged by the analysis of the data using the components resulting from the PCA. Correlation analysis of the components revealed a positive association between global and local processing in the visual domain. A relationship between verbal processing and visual

global processing was suggested by a trend in the correlation. After splitting groups, the positive relationship between global and local processing persisted only in the ED groups but not in the HC groups. This suggests that in the latter group these two dimensions may be independent.

The positive relationship between local and global processing in ED groups did not support the predictions of the central coherence account and adds to the argument against the unitarity of the concept of weak central coherence. However, these results need to be taken with caution as factors were extracted based using the whole sample of participants of this study, with only 25% corresponding to a HC group.

The inspection of the distribution of the data within groups for each factor helped to clarify relationships between factors. Statistical analysis showed that groups varied in the frequency of poor and good performance particularly in the verbal and global factors where the disadvantage for the ED groups was evident in comparison with the HC group. In the local processing factor no difference was found between groups but it was possible to extract from the graphs the superiority of BN and EDRec groups. The AN group, although better than the HC group did not show an outstanding performance in detail processing, suggesting that there might be confounding factors that may interfere with the efficacy of detail processing such as the level of starvation. In general, the profile of the data resulting from the PCA mirrors the analyses presented in the previous sections in terms of differences between groups. A more strict analysis of who has weak central coherence was derived from the combination of factors scores (under the 50<sup>th</sup> percentile in detail, and over the 50<sup>th</sup> percentile in verbal and visual coherence). Only 29.4% of the ED groups fulfilled the criteria versus a 16.7% in the HC group. Therefore, although the trade-off relationship between global and local processing was not common for all ED and HC participants, it was relevant for a third of the ED group.

In sum, the results suggest that good local processing is not necessarily achieved at the expense of global processing although a trade-off relationship between local and global processing is seen clearly in a third of the individuals in the ED groups. Finally, there is insufficient evidence in favour of cross-domain coherence. Bigger sample sizes may be required to clarify the potential association between factors found here.

## 7.5 Are Autistic-type Traits Related with Central Coherence?

### 7.5.1 Introduction

Weak central coherence has been described as a predominant cognitive style in ASD. Although not all the individuals exhibit the trait, the most conservative figures claim that at least a half of them would present this bias toward detail processing (Jarrold and Russell, 1997, Teunisse *et al.*, 2001).

As seen in previous chapters, there is some evidence in favour of a link between ED and ASD and, in fact, such a relationship has been proposed for more than 25 years (Gillberg, 1983). Similar characteristics to the typical information processing found in the ASD population have been described in ED, particularly in some studies in AN. These include difficulties in set-shifting and in the balance between local/global processing (see Chapters 1 and 2 of this thesis for details). Similarities in the anxious, compulsive phenotype and social/interpersonal functional impairments have also been reported (Crane *et al.*, 2007, Gillberg and Rastam, 1992, Zucker *et al.*, 2007). Deficits in Theory of Mind, one of the core characteristics of people with ASD (Baron-Cohen, 2004, Pellicano *et al.*, 2006), were found in AN in a higher proportion than in HC (Tchanturia *et al.*, 2004b). Moreover, a longitudinal study found that a group of women with AN actually met diagnostic criteria for ASD and that a disorder of empathy, typically seen in ASD, was also common in some patients with AN (Gillberg *et al.*, 2007, Gillberg *et al.*, 1994b, Rastam *et al.*, 1997, Wentz *et al.*, 1999).

Apart from the aforementioned series of studies conducted by Gillberg *et al.* that used a comprehensive individual assessment, there are no other studies that have looked at the convergence between neuropsychological function and autistic traits in ED.

In a recent study using self-report measures that have been extensively used in normal and ASD populations (Baron-Cohen *et al.*, 2003, Baron-Cohen and Wheelwright, 2004, Baron-Cohen *et al.*, 2001, Wheelwright *et al.*, 2006), no differences between AN and a healthy control group were found in empathy (EQ) and drive for systemizing (SQ). However, the AN group scored significantly higher in the AQ (autistic-like traits) (Hambrook *et al.*, 2008). Although most of the sub-scales of the AQ were found to be significantly higher in AN, only a trend was found

in the ‘attention to detail’ sub-scale which may relate to weak central coherence. As far as we are aware, there is yet no such study looking at autistic-type of traits in BN.

In this section, the objective is to add to the ‘bigger picture’ understanding of the weak central coherence account in ED combining neuropsychological and self-report data assessing autistic type traits (the Autism-Spectrum Quotient) and to see whether there is a link between weak central coherence and autistic traits in ED. The hypothesis is that weak central coherence indices (difficulties in global processing and strong local processing) would relate to higher indices of autistic traits which would be present in the ED groups. Specifically, it was expected that the attention to detail sub-scale of the AQ would correlate with weak central coherence indices. A secondary objective is to explore the presence of autistic-type traits among ED population in comparison with a HC group.

#### **7.5.1.1 Method and Data Analysis**

For this brief study, data from the previous PCA and the self-report measure of Autism-Spectrum Quotient (AQ) (Baron-Cohen *et al.*, 2001, Woodbury-Smith *et al.*, 2005) were combined in a series of correlational analyses. The AQ measure was described in the General Methodology Chapter of this thesis. In brief, it assesses autistic tendencies in response to 50 questions that investigate 5 areas related to the diagnosis of autism: social skills, attention switching, attention to detail, communication and imagination. The maximum score is 10 per scale and higher scores reflect a stronger presence of autistic traits.

The self-report measure was given to participants together with the other self-report measures used in this thesis. The majority but not all of the participants returned the questionnaire (AN = 38, BN = 42, EDRec = 42 and HC = 41).

Descriptive statistics of the AQ results are provided per group and a between group comparison was also performed with one-way between-groups ANOVA or Kruskal-Wallis according to data distribution.

### 7.5.1.2 Results

#### AQ profiles

Women with current ED did show higher scores in the overall AQ scale relative to the HC group. No differences between the recovered group and HC group were found except in the attention switching sub-scale whereby the EDRec group scored higher than the HC group. Results displayed per scale and groups are shown in Table 7.7.

The group with current AN displayed the highest scores among groups in all the scales Figure 7.7. Looking into individual between-group comparisons, AN was also the only group that scored significantly higher than the HC group in all the scales including both cognitive and social-communication features. Effect sizes varied between  $d = .72$  (medium effect size) in the communication scale and  $d = 1.3$  (huge effect size) in the attention switching scale. In the attention to detail sub-scale the effect size was medium ( $d = .71$ ).

**Table 7.7 Autism Spectrum Quotient (AQ) results in ED and HC groups**

Autism Spectrum Quotient sub-scales	AN <i>n</i> = 38	BN <i>n</i> = 42	EDRec <i>n</i> = 42	HC <i>n</i> = 41	$\chi^2$ <i>df</i> =3	<i>F</i> (3,159)	<i>p</i> -value	Post-hoc and between group comparisons <sup>c</sup>
Social Skills <sup>a</sup>	4 (2.8-8)	3 (1.8-6.3)	2 (1-5)	2 (1-4)	13.97	n.a.	.003	AN>HC
Attention Switching <sup>a</sup>	7 (5.8)	5 (3-7)	5.5 (4.7)	3 (2-5)	33.08	n.a.	<.001	BN, AN, EDRec>HC
Attention to Detail <sup>b</sup>	6.2 (2.2)	5.4 (2.5)	5.3 (2.2)	4.6 (2.3)	n.a.	2.86	.039	AN>HC AN=BN=EDRec
Communication <sup>a</sup>	4 (2-4)	3 (1.8-2.3)	2 (1-3.2)	2 (1-3)	15.27	n.a.	.002	AN, BN>HC
Imagination <sup>a</sup>	3 (2-4)	3 (1-3)	2 (1-3)	2 (1-3)	9.8	n.a.	.020	AN>HC
AQ total <sup>b</sup>	24.8 (8.2)	20.2 (7.7)	18.3 (5.6)	15 (6.9)	n.a.	12.94	<.001	AN>BN>HC=EDRec

<sup>a</sup>= Data non-normally distributed, median and upper and lower quartiles are reported (*Q*25-*Q*75)

<sup>b</sup>= Data normally distributed, means and standard deviation (SD) are reported

<sup>c</sup>= For normally distributed data one-way between-groups ANOVA was used with Tukey HSD post-hoc comparisons. In case of non-normally distributed data, Kruskal-Wallis tests were followed by Mann-Whitney U tests to compare HC with ED groups by separate and confirmed with rank sums test. New alpha value for significance after Bonferroni adjustments was set at  $p < .017$ .

n.a.= not applicable



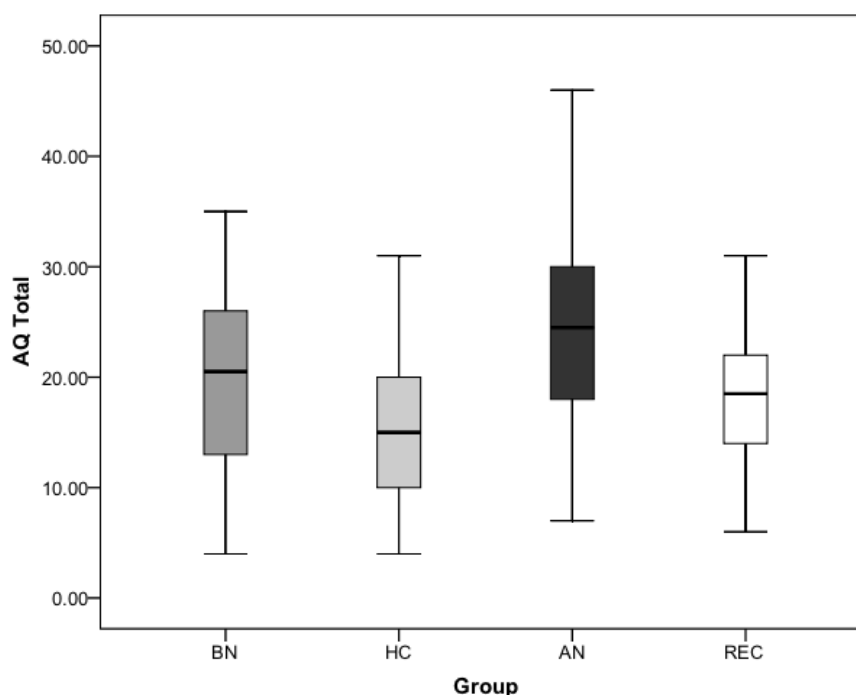
The BN group scored significantly higher than the HC group in the total AQ ( $d = .71$ ), attention switching ( $d = .74$ ) and communication ( $d = .58$ ) sub-scales. The difference with HC in the attention to details sub-scale did not reach statistical significance and the effect size was small ( $d = .29$ ).

It was interesting that the recovered women only differed from the HC in attention switching ( $d = .82$ ). In the attention to details sub-scale they scored similarly to the BN group and in the comparison with the HC the effect size was small ( $d = .30$ ). In light of these results in which autistic traits seem to be overrepresented in AN, we investigated the association between BMI, age and duration of the illness with AQ scores. A significant small correlation was found between BMI and total AQ score, attention switching and imagination (all  $r_s$  between  $-.17$  and  $-.25$ , all  $p < .05$ ). These findings suggest that lower BMI was linked to a higher rate of autistic type traits. Age and duration of the illness did not correlate with any sub-scale of AQ.

In terms of relationships between sub-scales it was surprising to find that attention to detail was the variable that held the lowest correlations with other sub-scales and the total AQ. This might be linked with the fact that this trait seems to be present across all groups at a high rate including the HC group and discriminates less well between groups. However, a positive relationship between attention to detail and attention switching was found ( $r_s = .27$ ,  $p < .001$ )

Finally, a cut-off score to discriminate between possible cases of ASD has been recently set at 26 points for the overall AQ scale (Woodbury-Smith *et al.*, 2005). According to this, 4 cases in the HC groups (9.8%), 3 in the EDRec group (7.1%), 12 in the BN group (28.6%) and 18 cases in the AN group (47.1%) met the criterion for a possible ASD. Pearson chi square revealed that differences between groups were significant ( $\chi^2 = 23.71$ ,  $df = 3$ ,  $p < .001$ ).

**Figure 7.7** Box plot of AQ scores in AN, BN, EDRec and HC groups



Relationship between AQ and central coherence factors

Bivariate Spearman’s correlation coefficients ( $r_s$ ) were calculated to test the strength of the relationship between all the AQ scales and verbal and visual global and detail factors obtained in the previous section.

The resulting correlations are listed below.

**Table 7.8** Correlations between AQ scores and central coherence factors

AQ sub-scales	Components		
	Visual Global Processing	Visual Detail Processing	Verbal Processing
AQ Total	-.198**	.056	-.234**
Social skills	-.104	.033	-.161*
Attention Switching	-.205**	.120	-.217**
Attention to Details	-.238**	-.097	.021
Communication	-.038	.161*	-.198*
Imagination	-.080	-.016	-.204**

\*\*  $p < .01$ , \*  $p < .05$

All the correlation coefficients were low indicating a weak strength in the relationship between central coherence factors and AQ sub-scales. However, the direction of the relationships and the fact that many of them were significant make these results of interest.

Correlation analyses showed that global processing skills (verbal and visual) are consistently inversely related with autistic traits. The two cognitive features measured by the AQ (attention to detail and attention switching) showed a significant association with lower levels of visual global processing skills which is in line with the weak central coherence account. Interestingly, in the case of the verbal coherence factor, the skills measured in the neuropsychological testing were associated with social or interpersonal functioning as well as with cognitive functioning (attention switching only). Finally, the visual detail processing factor was only significantly correlated with communication (higher scores in communication difficulties correlated with higher scores in detail processing). All the other correlation coefficients were extremely low and not significant indicating a lack of association between better detail processing and autistic traits in this study.

An inspection of those cases that scored over the cut-off for ASD in all the four groups uncovered a low strong association between verbal coherence and social skills ( $r_s = .332, p = .045$ ).

### **7.5.1.3 Conclusions**

This section addressed the question of whether weak coherence factors relate to autistic-type traits as measured by the Autism Spectrum Quotient (AQ) and a investigation of ASD traits in ED subtypes.

First, an analysis of the presence of autistic traits in the ED group was performed. The AQ was able to discriminate between women with current ED and women recovered or healthy. The group of women with AN presented the highest rate of autistic trait across all the sub-scales of the test. Moreover, almost half of the women belonging to this group scored over the cut-off point for ASD which suggests that they may have a disorder of the autistic spectrum. The only difference between healthy women and those recovered from an ED was in the attention switching sub-scale in which the EDRec group had similar score to the BN group. These patterns of

scores suggest that women with active AN display characteristics usually seen in people affected by an ASD such as poor social skills, poor communication skills, poor imagination, exceptional attention to detail and poor attention-switching or strong focus of attention. Cases with active BN have attention switching and communication skills lower than in the HC. In this small study, higher scores in AQ were associated with lower BMI. In light of these results it may be arguable that autistic-like features observed in the active phase of AN (Zucker *et al.*, 2007) are in part explained by the level of starvation that accentuates pre-onset characteristics and reduces after recovery. However, cognitive aspects may remain after recovery. Once recovered, women with ED seem to remain impaired only in the ability to shift attention which is in line with neuropsychological studies that support the enduring quality of set-shifting difficulties after recovery (Tchanturia *et al.*, 2004c).

In terms of the primary objective of this section, an inverse relationship between autistic traits and global processing abilities in both modalities (verbal and visual) was found. The only aspect that was associated with better local processing was poor communication skills. The sub-scale of attention to detail hypothesised to be related to indices of weak central coherence (low global and high local processing) was negatively correlated with global processing skills, i.e. the better the attention to detail the lower the ability in global processing, in line with the weak central coherence account. Finally, the relationship between attention to detail and attention switching found here supports the idea that these cognitive features interact.

Despite these interesting conclusions it is worth noting that the attention to detail sub-scale was the one that discriminated the least between groups. This relative lack of power may be due to the high scores for this scale in all the groups and not only in those affected by ED. Higher relative scores in this sub-scale in comparison with the other sub-scales of the AQ have been reported in previous studies in the general population (e.g. Baron-Cohen *et al.*, 2001). Moreover, it has been suggested that the detail sub-scale corresponds to a separate, independent factor from the other four subscales of the questionnaire (Hoekstra *et al.*, 2008).

It is necessary to mention that methodological issues limit the conclusions obtained from this section. A self-report questionnaire, although highly valid in the study of phenotypical traits of the autistic spectrum disorders (Woodbury-Smith *et al.*, 2005), has constraints when working with individuals who may have reduced self-awareness, as in the case of ED. A more appropriate design would include a

diagnostic interview for ASD (e.g. SCID), questionnaires to other informants (e.g. parents) in addition to the neuropsychological battery.

## **7.6 Getting the ‘bigger picture’**

The objective of this chapter was three fold. Firstly, to provide a summary of the data obtained in this study by a comparison of weak central coherence indices across the four groups involved in this thesis. Secondly, to test the unitarity of the concept of weak central coherence in ED, and thirdly, to explore whether factors associated with weak central coherence were related with autistic-type traits in the ED population.

The overall aim was to aid the understanding of the weak central coherence account in ED. In order to achieve this goal, a series of small studies looking at the available data from different perspectives were conducted. The only new data added to this section were the results from the Autism Spectrum Quotient, a self-report measure probing autistic traits (Baron-Cohen *et al.*, 2001).

The results from these studies corroborated the conclusions reported in previous chapters that the cognitive trait of weak central coherence is over-represented in women with current or past eating disorders in comparison with a healthy control group. The overall profile between women with active AN and BN as well as those recovered from the disorder differed only minimally in the central coherence profile resulting from either the individual analysis of the tasks used in this study or the component analysis derived from the general data. A more detailed analysis of the data revealed, however, a few discrepancies between the normal weight groups (BN and EDRec) and the AN group. The main differences were in the superiority in local processing which was higher in groups with normal weight and in the verbal coherence tasks in which normal weight ED groups performed poorer than AN. A weak but still existing relationship between superior local processing and BMI suggested that effects of starvation may impair the efficacy of local processing typically present in women with ED. The relatively poorer performance in verbal coherence tasks in the BN and EDRec groups would require further investigation and may respond to variations within the ED phenotype.

The question of the unitarity of the concept of central coherence was addressed through the performance of a Principal Component Analysis (PCA). The

main conclusions from this analysis were, the suggestion that good local processing is not necessarily achieved at the cost of poor global processing and, that the tasks used in the study seem to address a common underlying mechanism (i.e. central coherence). With regards to the first conclusion, the expected trade-off between local and global abilities was found in around a half of ED participants but not in the overall sample. This is partly in line with studies in the ASD population that have argued that the trade-off is more common in ASD but not in typically developing comparison groups (Booth, 2006, Mottron *et al.*, 2003, Teunisse *et al.*, 2001). The small association between the three factors resulting from the PCA supported the second conclusion, although the association between the verbal coherence factor and visual global processing reached only a statistical trend. Therefore, there was insufficient data to support or refute the cross modality question. A study with bigger sample size would be needed to clarify these relevant issues in the study of the concept of central coherence which is also yet to be solved in the study of ASD (e.g. Booth, 2006, Burnette *et al.*, 2005, Jolliffe and Baron-Cohen, 1999, Pellicano *et al.*, 2005, Teunisse *et al.*, 2001).

Another important finding of these studies was that weak central coherence, although common in ED, was not universal i.e. around half of the cases exhibit the trait but combinations between local and global abilities were spread out in the whole sample. Similar proportions of positive cases with weak central coherence have been found in the ASD literature. For example, Teunisse *et al.* (2001) reported that 57% of the ASD group had the trait comparable with the 55% found by Jarrold and Russell (1997). An unpublished study in ASD found that 47% of the individuals had weak central coherence in comparison with only 6% in the HC group (Loth *et al.*, unpublished). The finding that all types of interactions between local and global processing were evident in the ED sample may reflect the heterogeneity of the ED population as discussed in Chapter 2.

Finally, the last study found that women with active ED exhibit higher scores than the recovered and healthy control group in a measure of autistic-type traits. Those with AN showed the most extreme profile of autistic traits with almost a half of participants scoring over the cut-off point for a possible ASD (Woodbury-Smith *et al.*, 2005). Of interest for the study of central coherence was the finding of a relationship between weak global processing and autistic tendencies supporting the relationship between autistic psychopathology and weak central coherence. The fact

that the most persisting autistic feature was poor attention shifting and that it was inversely related to global processing is indicative of the importance of looking at the interaction between cognitive set-shifting abilities and weak central coherence. It might be possible that the difficulties seen in global processing are in part related to the impaired ability to switch between local and global abilities to respond to task demands. This hypothetical interaction between weak central coherence and executive functions, also suggested in the field of ASD (Happé and Frith, 2006), would be a good starting point for future investigation and may have implications for clinical practice.

## **8 THE CENTRAL COHERENCE ACCOUNT TRANSLATED INTO CLINICAL PRACTICE: THE DEVELOPMENT OF A MODULE OF COGNITIVE REMEDIATION THERAPY**

### **8.1 Introduction to the chapter**

This chapter presents an outline of the development and implementation of a novel module of intervention specifically designed to target the concept of weak central coherence in the treatment for patients with severe AN.

The chapter is divided into three sections. In the first section, the background to the development of interventions focused on cognitive information processing is provided. In the second section, the development of a module of Cognitive Remediation Therapy (CRT), that includes specific techniques to address difficulties in global processing, is described. Finally, in the third section, results from a pilot study of CRT carried out in the inpatient unit for AN of the Bethlem Royal Hospital in London, are presented.

Both the CRT module aimed at enhancing global processing and the results of the intervention described here are part of a bigger pilot study led by Dr. Tchanturia<sup>13</sup>, looking at the effectiveness of a module of CRT tailored to address the specific cognitive impairments that patients with AN often exhibit, such as difficulties in cognitive flexibility (set-shifting) and weak central coherence (see Chapter 1).

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<sup>13</sup> Dr. Kate Tchanturia, Senior Lecturer at the Institute of Psychiatry, King's College London, is second supervisor of this thesis and has led neuropsychological research in ED and developed a CRT module for AN.



## 8.2 Background and Development of the Study

### The need for aetiological and evidence-based treatments

Psychological and psychopharmacological treatment outcomes for adults with AN are poor (Bulik *et al.*, 2007a). Indeed, not a single study was graded “A” in the last guidelines of the National Institute for Clinical Excellence (NICE, 2004) and only one study reached the “B” quality criteria <sup>14</sup>.

There might be a number of possible reasons as to why outcomes are extremely poor in adults with AN as opposed to BN or adolescents with AN. In BN, for example, CBT is the treatment of choice with a large evidence base supporting its use (NICE, 2004) and medication has also been found useful (Shapiro *et al.*, 2007). A variety of family treatments for adolescents with AN have been supported by research as well (Bulik *et al.*, 2007a).

In order to improve the disappointing scenario for AN treatment, there has been a call to develop interventions that focus on addressing both risk and aetiological factors as well as evidence-based maintenance models (Cooper, 2005, Treasure, 2007). As mentioned in the introduction of this thesis, maintenance factors are particularly important for developing treatment strategies, as these are variables that predict symptom persistence over time among initially symptomatic individuals. Thus interventions specifically tailored to address maintenance factors such as those described in the Maudsley model for AN (Schmidt and Treasure, 2006) are hope to improved treatment outcomes. As a reminder, in the aforementioned model (see Chapter 1 for details) includes perfectionism and obsessive-compulsive personality traits (OCDP) within the four main maintaining factors for AN. This first maintenance factor is the main focus of interest for the present chapter. People suffering from AN typically present OCDP traits (Anderluh *et al.*, 2003), which have been linked with poor treatment outcomes in AN (Crane *et al.*, 2007). Recently,

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<sup>14</sup> NICE guidelines provide evidence-based recommendations for the treatment and management of physical and mental disorders. The grading scheme for these recommendations divides them into Grade A; B and C recommendations according to the quality of the studies supporting a specific procedure or treatment. Grade ‘A’ refers to the existence of at least one randomised controlled trial (RCT) as part of a good quality body of evidence supporting the recommendation; Grade ‘B’ refers to well conducted clinical studies in absence of RCT; and Grade ‘C’ are recommendations based on committees of experts’ opinions or reports of clinical experiences by authorities in the field (in absence of clinical studies of good quality).

Anderluh and collaborators have also demonstrated that OCPD traits shape the course of ED over lifetime (Anderluh *et al.*, 2008). Moreover, Treasure (2007) have proposed that perfectionism and cognitive ‘rigidity’ which are associated with obsessive-compulsive personality traits, may be underpinned by a rigid and detail focused thinking style. Thus, weak central coherence may act as an underlying maintenance factor of the illness facilitating the expression of phenotypic traits that can hinder progress in traditional psychotherapies (Southgate *et al.*, 2005a).

In consequence, the Maudsley model predicts that interventions that translate findings from neuropsychological studies, such as those presented in Chapters 4 to 6, to clinical interventions may help to reduce perfectionism and cognitive rigidity which in turn will result in symptom improvement. Overall, we proposed that in this form, intervention addressing underlying traits to ED psychopathology would to facilitate the progress of recovery, improve treatment outcomes and prevent relapses.

#### Translating neuropsychological studies into treatment: Cognitive Remediation Therapy

It has been argued that factors such as poor nutrition and low weight may interfere with the effectiveness of medication and the ability to process information in psychotherapy which in turn would affect outcomes (Bulik *et al.*, 2007a). Moreover, although weight gain improves some aspects of cognitive functioning, such as problem solving, attention, and processing speed (e.g. Kingston *et al.*, 1996, Lauer *et al.*, 1999, Moser *et al.*, 2003, Szmukler *et al.*, 1992, Tchanturia *et al.*, 2004c), some others remain unchangeable even after recovery, such as cognitive inflexibility (Tchanturia *et al.*, 2004c) and weak central coherence (see Chapter 6 and Gillberg *et al.*, 2007).

One possibility is that cognitive impairments that are present in people with AN and remain stable after weight gain may impede their ability to use the available treatments optimally as well as their motivation for taking up psychological treatments (Tchanturia and Hambrook, *in press*).

Our group have highlighted the importance of incorporating strategies that target these traits into the treatment for AN (Southgate *et al.*, 2005a).

The development of interventions based on the remediation of information processing styles of AN is somewhat new in the field (Baldock and Tchanturia, 2007). However, great advances have been achieved in other psychiatric disorders.

For example, forms of cognitive remediation have been developed for people with psychosis, brain injuries, attention deficit hyperactivity disorder and obsessive-compulsive disorder with promising results (Buhlmann *et al.*, 2006, Cicerone *et al.*, 2005, McGurk *et al.*, 2007, Park *et al.*, 2006, Stevenson *et al.*, 2002, Wykes and Reeder, 2005, Wykes *et al.*, 2007).

The theoretical rationale for this kind of treatment is that cognitive exercises, teaching and practicing cognitive skills, improve mental functioning and meta-cognition (*'thinking about thinking'*), which in turn promote self-regulatory function, adjusting cognitive processing according to environmental demands, and encourage the transference of cognitive skills into new situations (Wykes and Reeder, 2005). Therefore, improvements in cognition would be postulated to lead to enhancement of general functioning outcomes (e.g. symptoms and social functioning). From a neurodevelopmental point of view, cognitive exercises help people to advance to later stages of cognitive development by enhancing basic brain processes, thus refining and strengthening neural connections (Tchanturia and Hambrook, in press).

In eating disorders, Tchanturia and collaborators have developed an intensive module of Cognitive Remediation Therapy (CRT) focused on one of the major impairments of cognitive functioning in AN, namely 'set-shifting' (see Chapter 1). This intervention has been piloted through a series of cases studies with promising results. Furthermore, it has been found to be acceptable and feasible to deliver (Davies and Tchanturia, 2005, Tchanturia *et al.*, 2007a, Tchanturia *et al.*, 2006b). This module has been recently extended to include the recent findings with regards to extreme attention to detail and weak global processing in AN (Gillberg *et al.*, 1996, Gillberg *et al.*, 2007, Lopez *et al.*, 2008b, Southgate *et al.*, 2007). This novel intervention has been piloted with a sample of 23 women with severe AN recently admitted to our inpatient service (Tchanturia *et al.*, 2008). The results of this study will be presented below.

### 8.3 The Intervention

It must be clarified that by the time of writing of the present thesis, CRT had been refined and adapted so as to target *both* set-shifting difficulties and weak central coherence. However, the present Chapter addresses the question of whether CRT improves global processing only. Set-shifting aspects will not be described as it is beyond the scope of this thesis and the efficacy of CRT to remediate cognitive inflexibility has been reported elsewhere (Tchanturia *et al.*, 2007a, Tchanturia *et al.*, 2008). Therefore, the following section of this chapter will only describe the part of Cognitive Remediation Therapy for AN that looks at central coherence.

#### 8.3.1 General content of the intervention

CRT for AN was developed by Dr. Tchanturia and collaborators based on the work developed for patients with schizophrenia (Delahunty and Morice, 1993) to address cognitive impairments of adult patients. It was created as a pre-therapy intervention aimed at particularly targeting the needs of patients who have been recently admitted to an inpatient specialist unit for eating disorders.

CRT consists of a manualised therapist-led intervention of 10 sessions lasting between 30 to 45 minutes, ideally delivered in a twice-a-week format. In each session, a combination of set-shifting and global processing tasks is utilised.

The global enhancing module was designed to train people on how to overcome a local processing bias through a series of cognitive exercises, reflection on cognitive styles, and use of behavioural experiments between sessions. The overall aim of CRT for AN is to practice cognitive strategies and skills in order to strengthen global cognitive processing or promote more balance between detail and global processing.

The components of the sessions are:

- (1) Reflection and discussion on the bias towards local or detail thinking style based on exercises in which this style becomes apparent.
- (2) Identifying weaknesses and strengths related to the use of this predominant cognitive style and how it applies to the patient's daily life. There is a discussion between therapist and patient on how a particular cognitive style might be useful in certain situations but not others (e.g.

extreme detail focused style is needed for proof reading but might be inconvenient when summarising the content of a film to a friend, through a short message by phone or email etc).

- (3) Learning and practicing global processing strategies and gradually attempting to transfer them to daily life.
- (4) Behavioural experiments in between sessions in which the use and practice of new learnt strategies are encouraged.

As a manualised intervention (Tchanturia and Davies, in press), CRT provides clear guidance to the therapist as to the structure and content of sessions but at the same time allows certain flexibility to individualise the intervention according to the characteristics and needs of a specific patient (e.g. it is possible to graduate the difficulty of exercises) making them individually-tailored and relevant, as well as challenging, encouraging, reinforcing and creative. In general, the organisational scheme presented in Table 8.1 is followed.

There are more than 15 types of exercises described in the manual and once the patients has been familiarised with them it is possible to do up to 10-12 different tasks during each session. Cognitive exercises that are appropriate to practice global processing strategies include, for example, 'geometric figures', the 'main idea', 'prioritising task' and some of the modified stoop tasks.

It is worth mentioning that discussion pertaining to food, concerns about weight and shape and emotional issues, is explicitly left out of the content of CRT. When these issues emerge during sessions, the therapist acknowledges them but rather than explore them in more detail refocuses the discussion on cognitive styles and may link their concerns to these cognitive styles, if appropriate.

**Table 8.1 General scheme of CRT sessions**

<b>Sessions</b>	<b>Main components</b>
Sessions 1-3	<ul style="list-style-type: none"><li>▪ Building up a collaborative therapeutic alliance</li><li>▪ Explaining the rationale of CRT for AN</li><li>▪ Introducing and practicing exercises to identify the predominant cognitive style</li><li>▪ Encouraging of making links between cognitive exercises and behaviours out of session</li></ul>
Sessions 4-6	<ul style="list-style-type: none"><li>▪ Mainly practicing cognitive exercises</li><li>▪ Reflecting of strengths and weaknesses of predominant cognitive style</li><li>▪ Designing behavioural experiments in session</li><li>▪ Practicing behavioural experiments between sessions</li><li>▪ Reflecting on the results and strategies learnt in the behavioural experiments and how to overcome obstacles</li><li>▪ Encourage a transfer of skills to daily life</li></ul>
Sessions 6-8	<ul style="list-style-type: none"><li>▪ Practicing cognitive exercises</li><li>▪ Greater emphasis on designing, practicing and discussing behavioural experiments than in earlier sessions</li><li>▪ Encouraging of making links between behavioural experiments and behaviours in real life</li><li>▪ Preparing for the end of CRT</li></ul>
Session 9	<ul style="list-style-type: none"><li>▪ Same as sessions 6-8</li><li>▪ Reflecting on and discussing strategies to maintain changes after CRT</li><li>▪ Reflecting on and discussing difficulties that might arise after CRT and how they could be overcome</li><li>▪ Introducing 'Good Bye Letter' exchange for next session: A 'Good bye letter' is a motivational strategy where both patient and therapist summarise and reflect on the experience of CRT, cognitive styles, new strategies learnt, main achievements, areas that need further reinforcement, maintenance of changes and provide some guidance on overcoming possible future obstacles</li></ul>
Session 10	<ul style="list-style-type: none"><li>▪ Exchanging and discussing 'Good Bye Letters'</li><li>▪ Ending CRT</li></ul>

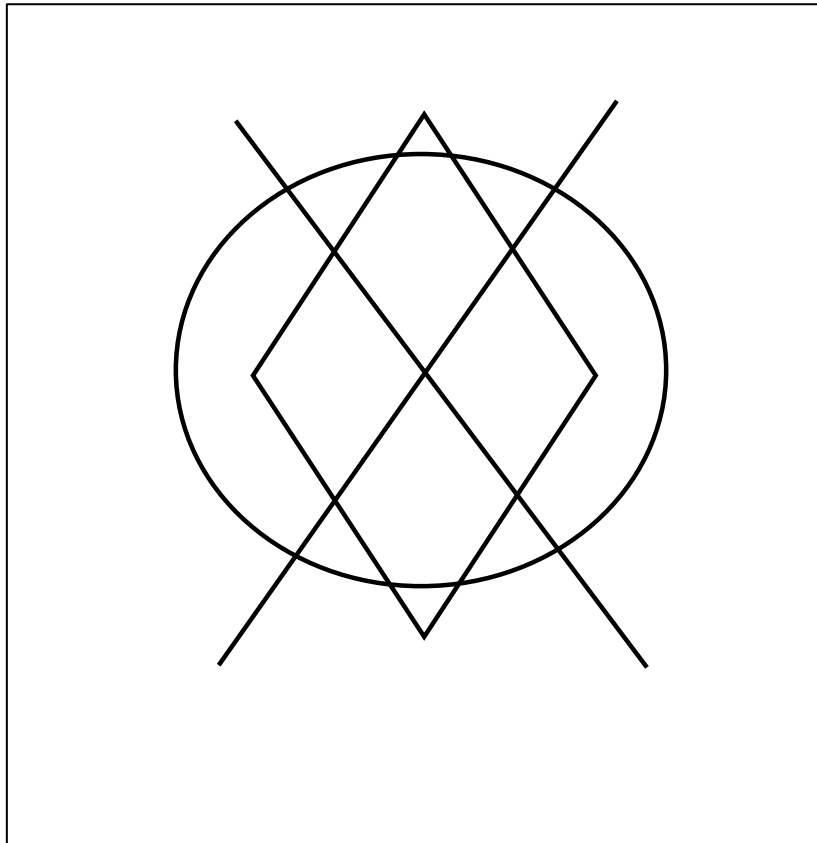
### 8.3.2 Global Processing Tasks

The aim of these exercises is to increase the use of global strategies when approaching different tasks as opposed to paying extreme attention to detail. These exercises involve developing a 'bigger picture' approach in the verbal and visual domains.

The following are examples of these tasks.

#### Geometric figures:

In this task the patient is asked to choose a diagram illustrating a complex figure from a set of such pictures (see Figure 8.1 as an example). The aim of the exercise is for the patient to verbally describe the diagram to the therapist who obeys the instructions and attempts to reconstruct the image. The therapist cannot see the picture until the patient has finished their description. After finishing the tasks therapist and patient reflect on the image the therapist has drawn and on the level of accuracy in comparison with the original diagram. The selection of global and more salient, primary, and relevant elements to describe the figure results in a more effective method of instruction and enables the therapist to draw a more exact replica of the complex figure. However, patients commonly use a detail-focused strategy to dictate how the figure should be drawn. An excessive focus on detail results in a poor replica of the figure, as instructions are difficult to follow and are less likely to lead to an integrated pattern when reproducing the picture. The therapist and patient reflect on this task by using a process of guided discovery aimed at thinking about the strategy used and of what would be the optimal strategy for the task. Therapist and patient can swap roles (e.g. therapist describes the figure and patient draws) so the therapist models the use of global strategies to the patient.



**Figure 8.1** An example of the Geometric Figures Task

The ‘main idea task’:

This task requires the patient to summarise a piece of written information by giving just the gist of the text. Patients are provided with a letter or an article from a newspaper or magazine, etc. and they are encouraged to extract the ‘main idea’ of the text. Some patients find this task extremely challenging. Therapist and patient discuss a number of strategies to make the task simpler: using bullet points, dividing the text into paragraphs and extracting the main idea from each paragraph first, trying to make up a title for the text, using visual diagrams, etc. In transferring these skills to real life, patients may practice composing shorter text messages on their mobile phone, getting to ‘the point’ when relaying events of the day or week to other people, etc.



### Prioritising task:

This task requires coming up with a hierarchy of priorities from a list of activities for the day or the week with the objective of encouraging patients to plan ahead with an integrative thinking approach).

Finally, some of the exercises target other relevant features for patients with AN such as perfectionism: in ‘estimation tasks’ the therapist encourages speed over accuracy. ‘Line Bisection’, for example, requires the patient to make swift, rough estimates of the midpoint of a line and to approximately mark these with a pencil. Motor multitasking tasks (e.g. asking the patient to draw ‘infinity signs’ using their non-dominant hand, both hands at once, closing their eyes as they draw), also promote a more playful, relaxed approach as accuracy and perfection are not the main goals.

### 8.3.3 Delivery of the intervention

CRT is offered to patients who have been recently admitted to the inpatient Unit for Eating Disorders at the Bethlem Royal Hospital. After an initial neuropsychological assessment a therapist is allocated to the patient. Therapists can be any mental health care professional provided they are given appropriate training and supervision. In the model presented here, therapists were in the main psychologists but social workers and nurses were also included. Therapists were trained and supervised by Dr. Kate Tchanturia on a weekly basis.

CRT starts typically within the first two weeks following admission. The completion of 10 sessions of CRT typically occurs 8 or 10 weeks after the first neuropsychological assessment.

## **8.4 Aims and Hypothesis of the Study**

The aim of this study was to examine whether an intensive module of CRT would have an impact on the display of global as opposed to detail focused strategies in neuropsychological testing. A secondary aim was to explore whether cognitive performance improvements relate to clinical symptomatology.

Accordingly, the hypotheses were that 1) women with severe AN would improve in the use of global processing strategies after 10 sessions of CRT training and that 2) these improvements would be related with improvements in clinical symptoms (e.g. levels of depression, anxiety, obsessive-compulsive symptoms and BMI).

## **8.5 Methods**

### **8.5.1 Design**

This study employed an observational prospective consecutive case series design. No control group was used.

### **8.5.2 Participants**

Twenty-three women with severe AN recently admitted to the inpatient Eating Disorders Unit of the South London and Maudsley NHS Foundation Trust between 2004 and 2007 took part in the study. The inclusion criteria were: recent admission to the hospital at the beginning of the CRT intervention, being physically stable, no past/current head injury, psychosis or severe learning disabilities.

### **8.5.3 Measures**

The test employed to evaluate central coherence was *The Rey-Osterrieth Complex Figure* (RCFT; Osterrieth, 1944) and coherence indices developed by Booth (2006) were used. Only the copy trial of the RCFT was used in this study because the aim was focused on examining the process of drawing only rather than the impact of memory, hence the recall trial was omitted. Additionally, using the copy trial only would help to reduce the potential of practice effects by decreasing exposure to the figure. A full description of these tests is provided in Chapter 3. The National Adult Reading Test was also administered (NART; Nelson and Willison, 1991).

Some self-report questionnaires to measure comorbid symptoms were used: The Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983) and the Maudsley Obsessional-Compulsive Inventory (MOCI; Hodgson and Rachman, 1977). The latter is a 30-item self-report questionnaire used to evaluate obsessive and compulsive behaviours and thoughts. The maximum score is 30 (one point per item) with higher scores indicating the presence of more behaviours and thoughts typically associated with an obsessive-compulsive disorder.

In addition to the battery of self-report measures, a treatment satisfaction questionnaire was given to patients to be completed after the 10 sessions of CRT. This questionnaire consisted of 6 items rated 0 to 10 by means of a visual analogue scale (VAS) and covered various aspects of the treatment (e.g. perceived effectiveness, usefulness, transferable skills, etc).

Data from the satisfaction questionnaire will only be considered in their relation to changes in global processing performance in order to focus on analyses that are relevant to the objective of this thesis.

#### 8.5.4 Procedure

The procedures of this study were approved by the Institute of Psychiatry/South London and Maudsley NHS Trust Research Ethical Committee (Study number 05/Q0706/315). Written informed consent was obtained from participants before commencing their participation in this study. Confidentiality of participants was assured at all stages. Participants were allowed to withdraw from the study at any time.

Patients were offered 10 individual sessions of CRT soon after they were admitted to the inpatient Unit at the Bethlem Hospital. Prior to commencing the intervention, patients were assessed in a single one-to-one session of neuropsychological testing by a trained researcher. Assessments were typically conducted within the two first weeks after admission and lasted about 45 minutes. Weight and height were obtained from medical notes. Self-report questionnaires were given to patients to fill out either in the testing session or at their own time following the session. After the assessment, a therapist was assigned to the patient and 10 sessions of CRT were delivered in a twice a week format. CRT therapists

were volunteers who had training in psychology, nursing or social work. They were all trained in the delivery of CRT and participated in weekly supervision provided by Dr. Tchanturia. Sessions were audio taped or video taped when possible. Once the CRT sessions finished, the same researcher who had conducted the baseline examination, carried out a second assessment using the same neuropsychological tasks. In general, post-intervention assessments were carried out at 8-10 weeks after baseline. It is important to mention that in CRT patients are not given feedback about their test performance to avoid any learning effects that might bias the second assessment results.

Two patients did not return the self-report MOCI and one did not return the HADS in the first assessment. In the post-intervention assessment one patient did not return both of these self-report measures. Finally, two participants did not fill in the satisfaction questionnaire.

#### 8.5.5 Data analysis

Analyses were conducted using SPSS Version 16. In order to detect whether the CRT intervention had an impact on the use of global strategies in the RCFT, results of baseline and post-intervention assessments were compared using neuropsychological and self-report data. Exploratory analyses were conducted to determine whether parametric or non-parametric statistics were appropriate. Paired sample *t*-tests were used for normally distributed data and their non-parametric alternative, the Wilcoxon Signed Rank Test, was used to compare baseline and follow-up measures. McNemar  $\chi^2$  Test was used to compare proportions of individuals who improved in global processing after CRT.

Cohen's *d* was calculated to obtain the effect size for each variable. Cohen's effect sizes are interpreted as *negligible* ( $= 0$  and  $<.15$ ), *small* ( $\geq.15$  and  $<.40$ ), *moderate* ( $\geq.40$  and  $<.75$ ), *large* ( $\geq.75$  and  $<1.10$ ) and *very large* ( $\geq 1.10$ ). To explore the associations between neuropsychological, demographic and clinical variables, Pearson's correlation coefficient (*r*) was used for normally distributed data and Spearman's rank (*r<sub>s</sub>*) correlation was used otherwise. The nominal significance level was chosen to be .05. Hochberg improved Bonferroni corrections were applied (Hochberg, 1988).

## 8.6 Results <sup>15</sup>

### 8.6.1 Demographic and Clinical Characteristics

Twenty-seven patients with AN were offered CRT soon after they were admitted to the inpatient Unit. Two of them refused to take part in the study and another two dropped-out after having completed five sessions of the intervention. Therefore the drop-out rate was 8%.

All participants were Caucasian females with severe AN (see Table 8.2). Sixteen of them had restricting AN (73.9 %) and 6 had binge-purge AN (26.1 %). Their mean age was 28.8 years ( $SD = 9.2$ ) and they had a mean duration of illness of 13.1 years ( $SD = 9.6$ ). Their average estimated intellectual ability was 112.7 ( $SD = 6.5$ ). Age data was non-normally distributed therefore median (*Mdn*) and lower and upper quartiles (Q25-75) are reported. The median age at onset was 15 years (14 – 17).

BMI and levels of co-morbid symptoms were compared pre and post CRT. The results are presented in the Table below.

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<sup>15</sup> Some of the results presented below are described in a manuscript entitled: 'Neuropsychological task performance before and after cognitive remediation in anorexia nervosa: A pilot case series', accepted for publication in *Psychological Medicine* (Tchanturia *et al.*, 2008)

**Table 8.2 Clinical characteristics of the participants at baseline and post CRT**

	<i>n</i>		T1	T2	Test statistic		<i>p</i> -value	Effect Size ( <i>d</i> )
	T1	T2			paired- <i>t</i> <sup>a</sup>	<i>z</i> <sup>b</sup>		
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	23	23	14.3 (1.4)	16.1 (1.5)	-7.4	n.a.	<.001	1.25
Anxiety HADS <sup>b</sup>	22	23	16 (13-19)	15 (12.8-19)	n.a.	-1.8	.08	.54
Depression HADS <sup>a</sup>	22	23	14.2 (3.4)	12.6 (4.8)	2.7	n.a.	.01	.36
MOCI <sup>b</sup>	21	22	13 (9.5-19.5)	12 (9.5-16.5)	n.a.	-0.5	.60	.14

T1 = Baseline assessment; T2 = Post-intervention assessment

<sup>a</sup> paired *t*-test = test statistics for paired *t*-test pairwise comparisons for data normally distributed, mean values displayed with standard deviations.

<sup>b</sup> *z* = test statistics for Wilcoxon Signed Rank Test for data not normally distributed, median values displayed with upper and lower quartiles.

n.a.= not applicable.

HADS scores before and after CRT were above clinical threshold (>10 points on each scale). By the time of the post-CRT assessment only depression had statistically significantly decreased. Anxiety levels also decreased but on a trend level only although effect size revealed a moderate improvement ( $d = .54$ ). No significant changes were observed on the MOCI. Significant results displayed in Table 8.2. remained significant after Hochberg corrections (Hochberg, 1988) for multiple testing ( $p < .05$ ).

### 8.6.2 Neuropsychological Function

In this section, baseline and post-CRT data are shown first, using a within group comparison. Then, a comparison with the healthy control group results obtained from the cross-sectional studies described in Chapters 4 through 6, is provided.

### 8.6.2.1 Baseline and post-CRT assessment results

After the intervention, participants significantly improved in the use of global strategies (central coherence index:  $t = -2.2$ ,  $p = .04$ ). Particularly, they reduced the fragmentation in their drawing style with a large effect size (style index:  $z = -2.4$ ,  $p = .01$ ). No changes were found in terms of attention to detail in the copy processing (Order index). The differences in the Style index remained significant after Hochberg corrections for multiple testing ( $p = .04$ ), however, differences in the general Central Coherence index fell to non significant levels ( $p = .12$ ) (Hochberg, 1988).

In terms of supplementary information provided by the test, patients showed similar accuracy in copying the figure at both times of assessment.

Table 8.3 displays the baseline and post-intervention assessment using the RCFT.

**Table 8.3 Global processing performance**

Rey-Osterrieth Complex Figure	<i>n</i>		T1	T2	Test statistic		<i>p</i> - value	Effect Size ( <i>d</i> )
	T1	T2			paired- <i>t</i> <sup>a</sup>	<i>z</i> <sup>b</sup>		
Order index <sup>b</sup>	23	23	2.33 (1.7-2.7)	2.33 (2.2-2.5)	n.a.	-.77	.44	.22
Style index <sup>b</sup>	23	23	1.5 (1.2-1.7)	1.7 (1.3-2)	n.a.	-2.4	.01	.75
Coherence Index <sup>a</sup>	23	23	1.35 (.42)	1.5 (.32)	-2.2	n.a.	.04	.42
Accuracy <sup>b</sup>	23	23	30 (26.5-33)	29 (23-32)	n.a.	-.82	.41	.24

T1 = Baseline assessment; T2 = Post-intervention assessment

<sup>a</sup> paired *t*-test = test statistics for paired *t*-test pairwise comparisons for data normally distributed, mean values displayed with standard deviations.

<sup>b</sup> *z* = test statistics for Wilcoxon Signed Rank Test for data not normally distributed, median values displayed with upper and lower quartiles.

n.a.= not applicable.

### **8.6.2.2 A comparison with a healthy control group**

As there was no control group in this study, it was difficult to infer the meaning of these results in terms of general functioning. Therefore, data obtained from a healthy control group (HC) in the previous studies described in this thesis, was merged with the data obtained from the CRT group in order to analyse and compare the results in global processing performance.

The HC group was equivalent to the CRT group (CRTg) in terms of estimated intellectual ability ( $t = -.30$ ,  $df = 46$ ,  $p = .76$ ). As expected, there was a difference between groups in BMI both at baseline and post-CRT (both  $p < .001$ ).

At baseline, order and style indices were examined with Mann-Whitney  $U$  tests for non-normally distributed data. The between groups comparisons revealed that groups were significantly different on style index (Mann-Whitney  $U$  Test = 315.0,  $z = -2.3$ ,  $p = .02$ ,  $d = .60$ ) and a difference on a trend level was found on order index (Mann-Whitney Test = 358.5,  $z = -1.7$ ,  $p = .08$ ,  $d = .43$ ). Independent  $t$  tests comparing CRTg scores on the general coherence index with the HC group scores showed that the CRTg scores were significantly lower than those obtained by the HC group, with a moderate effect size ( $t = 2.9$ ,  $p = .005$ ,  $d = .72$ ). However, after CRT, differences between groups diminished. Mann-Whitney  $U$  tests showed that the scores in Order and Style indices were statistically equivalent to the HC group with moderate and negligible effect sizes, respectively ( $z = 1.5$ ,  $p = .12$ ,  $d = .39$  for Order index and  $z = -.17$ ,  $p = .87$ ,  $d = .04$  for Style index). Similarly, no differences were found on the general Coherence index ( $t = 1.23$ ,  $p = .21$ ,  $d = .32$ ).

These results show that after CRT, the CRTg group approached the scores obtained by a sample of healthy controls. However, the small sample size may have precluded the identification of statistically significant differences between groups, particularly on the Order index (moderate effect size).

### **8.6.2.3 Another look at the data**

In this study there was no selection of participants according to their scores on central coherence indices in the first assessment and all patients were included although some did not show substantial impairments in global processing at the time of the first assessment. This in effect may have obscured the possibility of finding bigger changes in global processing performance after CRT sessions.



To explore these observations further, a comparison of the proportions of individuals in the CRTg group who scored lower than the 25<sup>th</sup> percentile (*Q*25) of the HC scores on each index (i.e. considered ‘impaired’ on the specific index), before and after CRT, was carried out using McNemar tests. The results of these analyses are shown in the table below.

**Table 8.4 Proportions of ‘impaired’ individuals on global processing of information at baseline and post-CRT**

RCFT index	% < <i>Q</i> 25 baseline	% < <i>Q</i> 25 post-CRT	McNemar $\chi^2$ <i>p</i> -value
Order Index <sup>a</sup>	52 % (n = 12)	47.8 % (n = 11)	.100
Style Index <sup>b</sup>	69.6 % (n = 16)	30.4 % (n = 7)	.03
Coherence Index <sup>c</sup>	56.5 % (n = 13)	43.5 % (n = 10)	.13

<sup>a</sup> = Index below 2.2 according HC data

<sup>b</sup> = Index below 1.5 according HC data

<sup>c</sup> = Index below 1.5 according HC data

The proportion of individual ‘impaired’ on the style index was significantly reduced after CRT sessions. However, no significant changes were found in the proportion of individuals who improved in their ability to resist focusing on detail (order index). The decrease in the proportion of ‘impaired’ individuals in the central coherence index did not reach levels of statistical significance.

These results thereby corroborate the conclusions that were described in the previous section.

Although set-shifting data are not included in this chapter, it is worth mentioning that improvements found in performance in set-shifting tasks were not associated with any changes in the performance on the RCFT, thereby supporting the independence of both concepts.

### 8.6.3 Relationships between demographic, clinical characteristics and improvements in global processing scores

Variables such as BMI, duration of illness and co-morbid symptoms were analysed in relationship with improvements on central coherence indices scores. As BMI and depression levels varied significantly from baseline to post - CRT assessment these changes were also investigated in terms of their association to improvements in central coherence.

Positive changes in BMI did not correlate with either the improvements on coherence indices or the full scores at baseline and post-CRT assessments. Improvements in depressive symptoms were not associated with increases in the coherence indices either. However, there was a negative relationship between depressive symptoms before CRT (full scores) and improvement in the Style index of the RCFT ( $r_s = -.438, p < .05$ ). Thus, people who were more depressed at baseline benefited less from the intervention in terms of reduced fragmentation in information processing. No other significant relationships were found.

### 8.6.4 Improvements in global processing and satisfaction with the treatment

The questionnaire for satisfaction with the treatment has 6 scales measuring the degree of satisfaction with different aspects of the treatment such as effectiveness of the intervention, whether the treatment met the patient's expectations, the provision of transferable skills, satisfaction with the number of sessions and length of sessions, etc. Generally speaking, 21 patients who completed CRT and answered the questionnaire reported being satisfied with the treatment received (scores over 5 in a 0 to 10 scale). The only aspect of the treatment with a score lower than 5 was the degree of importance that patients gave to including close relatives in the intervention (average score was 3.6,  $SD = 3.0$ ). The most highly endorsed elements were 'positive feelings about the intervention' and 'meeting expectations' of the patient (average score  $> 6.6$ , for both).

Correlation analyses were carried out between the degree of satisfaction with these aspects of the treatment and improvements in the coherence indices. Improvements in style index of RCFT and general coherence index were related to the perceptions that expectations were met by the treatment ( $r_s = .63, p = .003$  and

$r_s = .53, p = .01$ , respectively). Also, the general coherence index was positively related with perceived effectiveness ( $r_s = .47, p < .03$ ) and with positive feelings with regards to the intervention ( $r = .46, p = .04$ ).

## 8.7 Discussion

The aim of this study was to examine the effectiveness of an intensive module of Cognitive Remediation Therapy (CRT) for severe cases of AN designed to increase the use of global processing strategies in neuropsychological testing and to explore whether any changes to this effect were related with clinical improvements and satisfaction with treatment.

The hypothesis that after CRT participants would improve in the use of global strategies was supported. Women with severe AN recently admitted to the hospital did use better global processing strategies in copying a complex figure (RCFT) after 10 sessions of CRT. This manifested as positive changes in the Style and Coherence indices of the RCFT, improvements on which had large and moderate effect sizes, respectively. Particularly, patients considerably reduced the segmentation in their drawing style, which reveals that main aspects of the figure were seen as wholes instead of disjointed pieces of information. However, the tendency to attend to details first rather than to more global elements of the figure when beginning to copy the figure did not show improvements. The above results were confirmed with further analysis that showed that the proportion of patients who had weak coherence (below the 25<sup>th</sup> percentile of a healthy population) was significantly reduced after CRT from 56.5 % to 43.5 %. It is noteworthy that only a half of this specific group of patients were extremely biased towards attention to detail in the initial stage of their drawing (Order index) which can partly explain the lack of significance of improvements in this area after the intervention.

These positive results are in line with the encouraging preliminary findings and clinical observations in using CRT in patients with AN (Pretorius and Tchanturia, 2007, Whitney *et al.*, 2008) as well as with results in other psychiatric illnesses, such as schizophrenia (Wykes *et al.*, 2007). Also, other interventions that focus on cognitive styles have been used in obsessive-compulsive disorders (OCD) with success. For example, Park and collaborators developed a cognitive training

programme for people with OCD which used the examination and practicing of versions of the block design task as the main training tool. Two groups of 15 OCD patients took part in the study in which one group received cognitive training and the other group did not receive such as intervention. The training group had a decrease in clinical symptoms and also improved their recall accuracy and organisational strategies in the RCFT (Park et al., 2006). Also Buhlmann *et al.* (2006) developed a brief module targeting organisational strategies in OCD with positive results in terms of improving test performance.

The intervention was also well received by patients who in the main found it useful, effective and acceptable. The patients' positive perceptions obtained from the satisfaction questionnaire were later corroborated in a qualitative study that looked at the 'good bye letters' written by 19 patients participating in the present study (Whitney et al., 2008). Qualitative data revealed that most of patients (17 out of 19; 89%) were satisfied with the treatment, and 63 % (12 out of 19 patients) would recommend CRT to other people, and most of them stated that they were able to incorporate new skills into their daily life. One possible explanation for such a good acceptance of the intervention may be the fact that one of the main characteristics of CRT as opposed to other traditional psychological treatments is that CRT does not directly target emotional issues and ED symptoms, in fact, those elements are explicitly left out of the main discussion in the sessions. This characteristic of the intervention makes CRT more receptive to patients who have had a long history of treatment and describe the intervention as 'refreshing'. However, for some patients this characteristic of the treatment makes it more difficult to identify the relevance of cognitive exercises for the recovery process i.e. understanding how cognitive exercises can help them to reduce ED symptoms.

Overall, the positive feedback from patients together with the fact that CRT helped to improve the use of global strategies both encourage further research into this type of intervention for AN. It is still unclear whether positive changes in global processing relate to ED symptoms or other clinical symptoms. Randomised Controlled Trials (RCT) and follow-up studies would help to better understand the effect of improving global processing skills on ED psychopathology and general functioning.

### Limitations of the study

There are some limitations in this study. Firstly, this was an exploratory pilot study and as such it lacks control conditions (e.g. repeated baseline measures or a control intervention). Therefore, the design of this study does not allow us to establish whether improvements in the use of global processing of information are a direct result of CRT training or other intervening factors, such as other interventions provided by the standard treatment in the inpatient Unit such as refeeding, nursing, occupational therapy, etc. However, a previous study conducted by Dr. Tchanturia in 2004 in the same inpatient Unit for AN and using the same battery of set-shifting tasks, suggested that cognitive functioning linked to these enduring traits, specifically cognitive inflexibility, does not improve with treatment as usual independently of significant increases in BMI (Tchanturia *et al.*, 2004c). However, the latter study did not include measures of global processing. In the present study we found that BMI did not relate to improvements in global processing which is in line with the argument that some aspects of the information processing does not improve with weight gain only (Tchanturia *et al.*, 2004c). Finally, there was no association between improvements in co-morbid symptoms and changes in coherence indices although it was found that for those who were more depressed at the baseline assessment the intervention was less beneficial. An RCT and the completion of the ongoing follow-up of the patients who took part in this study, would help to clarify these effects.

Secondly, the sample size may have been insufficient to detect significant changes in some of the variables measured. For example, positive changes in Order index may have needed a bigger sample size, as well as taking into account that patients were not significantly impaired in this dimension at the baseline assessment.

Thirdly, only one visual-spatial task was used to measure central coherence in this study (RCFT). This fact limits the examination of possible improvements in other domains also targeted in CRT (e.g. verbal domain). It has also been argued that the RCFT is an open-ended task i.e. a task where the individual spontaneously expresses their predominant cognitive style given that taking either a global or local approach does not relate directly to task success (Booth, personal communication). Therefore, it is possible that in some of the cases, improvements in global processing were not detected on this task, as the individual is not forced to take a global approach to successfully copy the figure. Thus, the RCFT might be somewhat

insensitive to improvements in global processing strategies. Having said that, the RCFT has been found to be sensitive enough to detect improvements in organisational strategies in the aforementioned small study involving two groups of OCD patients (Park *et al.*, 2006). In any case, a task that specifically proves a deficit in global processing may therefore be useful in future studies. One promising possibility is the Fragmented Pictures task (Snodgrass and Corwin, 1988, Snodgrass *et al.*, 1987). This task has been used to assess weak central coherence in individuals with ASD. Booth's study (2006) showed that individuals with ASD, thought to have weak central coherence, were significantly impaired in their ability to integrate fragments of information when identifying familiar single objects, compared with a healthy control group.

Fourthly, forms of cognitive remediation have been used in other psychiatric disorders (e.g. Park *et al.*, 2006, Stevenson *et al.*, 2002, Wykes and Reeder, 2005). In these cases, along with the neuropsychological positive changes, cognitive training benefits clinical and general functioning. In CRT for AN only depression levels and BMI improved significantly during the course of CRT but these improvements were not associated with the changes in global processing strategies. Other aspects of general functioning (e.g. quality of life or social functioning) were not examined in this study therefore we were unable to explore these possible relationships. Future studies may need to include measures to address general functioning and other measures of ED outcomes in order to answer the question of the clinical relevance of including CRT as part of the treatment for AN.

Finally, the same tasks were used for both baseline and post-CRT assessments. It might be possible that practice effects occur and that they explain part of the changes observed here (Szoke *et al.*, 2008). This is one of the main difficulties in treatment research, especially when using neuropsychological tests. There are, however, different ways of addressing this difficulty. One possibility is using alternative forms of the tasks as long as they have been carefully validated as comparable measures. The Taylor figure (Taylor, 1969) was a good candidate as an alternative to the RCFT. However, in its original form it has been criticised as being easier than the RCFT (Gagnon *et al.*, 2003, Hubley and Tremblay, 2002, Strauss *et al.*, 2006). A modified Taylor figure with an equivalent level of difficulty as the RCFT in terms of memory, learning and copy performance, has been developed (Hubley and Jassal, 2006, Hubley and Tremblay, 2002, Yamashita, 2006) and might

benefit future research. However, as yet no one has investigated the comparability in terms of drawing style process outcomes. In the present study, in order to reduce the possibility of practice effects, the copy trial alone was used (omitting immediate and delayed recall). Also, no feedback was elicited or provided about performance on the task.

### Strengths of the study

This study also has a number of strong points. First of all, this is the first study, as far as we are aware of, to test the effectiveness of an intervention that directly targets cognitive functioning in patients with AN.

Secondly, having said that the sample size might have been insufficient to detect bigger changes on the global processing tasks, twenty-three patients completed the study which is a respectable size for a pilot study involving therapeutic interventions in ED and only 8% of the original sample dropped-out which is lower than the usual rates for treatment in severe cases of AN (Halmi *et al.*, 2005b).

Thirdly, the design of the study included procedures aimed at standardising the intervention and assessment procedures as much as possible as well as minimising researcher and selection biases. Thus, the study did not exclude the most severe cases except if conditions such as psychosis were present. The assessors were researchers with training in neuropsychological assessment and the same researcher carried out the baseline and post-CRT assessments for a patient, as well as the scoring and entering of the data. The administration of the RCFT was video-recorded when possible. The assessor/researcher was always different than the allocated therapist. Therapists were blind to the results of the assessment in order to prevent bias in the delivery of the intervention. Finally, although used with flexibility, the intervention was manualised, and weekly group supervision was provided.

Lastly, as this study shared the main outcome measure with the studies previously described in this thesis, it was possible to compare present results with those of a healthy control group. Although this type of comparison has methodological limitations, it helps to put the results obtained by the participants of this study into context.

## 8.8 Conclusion

This pilot study was aimed at evaluating the effectiveness and acceptability of a module of Cognitive Remediation Therapy (CRT) for patients with severe AN. Specifically, the results presented here illustrate the impact of cognitive exercises that aim to enhance the global processing difficulties that are typically exhibited by this type of patients.

The study showed promising results. After CRT patients had improved significantly on at least one aspect of visual coherence as measured by the RCFT. Patients tended to make more use of global strategies to copy the complex figure, specifically in terms of reducing fragmentation in their drawing style. The preference for attending to details over global aspects of the figure was not particularly marked at baseline and did not change significantly after the sessions. Importantly, the general profile of patients' results after CRT on the indices of central coherence on the RCFT was closer to that found in a healthy control sample described in previous chapters of this thesis. Finally, the intervention was acceptable and valued by patients and some of the satisfaction indices were related to improvements on central coherence indices.

Thus, it seems that the inclusion of interventions that directly address cognitive traits, such as weak central coherence that may underlie obsessive-compulsive traits, widens the options available within treatment and may help to overcome the current difficulties in treating AN patients and improve both acceptability of treatment and treatment outcomes.

Elements such as improvements in global processing, good acceptability and satisfaction with the intervention as well as low drop-out rate encourage further advances in this type of interventions and support the development of future research involving CRT for AN.

How CRT may be incorporated into an effective treatment package is still uncertain. One possibility is to offer CRT as pre-therapy module that facilitates the effectiveness of further, more complex psychotherapeutic interventions (Pretorius and Tchanturia, 2007). CRT might not be suitable as a stand-alone therapy due to the clinical characteristics of the patients that would receive this intervention. However, a shorter version of CRT may also be of use in out-patient settings (Baldock and Tchanturia, 2007).



Future CRT studies may help to understand the added value of such an intervention within the general context of AN treatment. Future studies might need to include control conditions and the exploration of the clinical relevance of these findings i.e. relationships between improvements in global processing and clinical outcomes and general functioning (e.g. social and educational/work life) as well as the long-term maintenance of changes after the intervention.

## 9 THE CENTRAL COHERENCE ACCOUNT TRANSLATED INTO CLINICAL PRACTICE: PART II. A BRIEF MOTIVATIONAL FEEDBACK INTERVENTION <sup>16</sup>

### 9.1 Introduction to the chapter

This chapter is linked to the previous one in that it relates to the clinical implications of the neuropsychological studies looking at central coherence in the ED population. The present chapter describes the development and implementation of another innovative intervention, specially designed for outpatient settings, that targets weak central coherence by shifting the focus from detail onto global processing.

The work was jointly developed with Professor Treasure, and involved the design of a new intervention to translate the neuropsychological assessment of weak central coherence into a feedback intervention as a module within the general New Maudsley model of treatment (Schmidt and Treasure, 2006). This intervention differs from CRT (see Chapter 8) in a number of ways that will be discussed later in this thesis. However, they are similar in that both address the *how* (process) rather than the *what* (contents) of thinking. This feedback intervention module is being piloted and refined through ongoing work. In its current form, the intervention involves feedback in both weak central coherence and set-shifting difficulties. The preliminary development of this short intervention, which only included assessment and feedback on weak central coherence, is described in the following pages. A published case report study has shown that this brief module offers valuable information to patients and is an acceptable and useful intervention (Lopez *et al.*, 2008d).

The chapter is divided into three parts. Firstly, the background for the intervention is provided. Secondly, a description of the intervention and its aims,

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<sup>16</sup> A version of this description has been accepted for publication in the European Eating Disorders Review under the title of 'Using neuropsychological feedback therapeutically in treatment for anorexia nervosa: Two illustrative case reports', (Lopez *et al.* 2008, doi: 10.1002/erv.866)

rationale and procedures, is given. Thirdly, a pilot exploratory study and its preliminary results are described.

## **9.2 Background and Development of the Study**

As mentioned in the previous chapter, treatment strategies that target the underlying cognitive traits that may help to maintain the illness seem to represent a non-threatening therapeutic tool that allows individuals to step back and understand why they get trapped by the disorder.

As far as we are aware, only CRT has used neuropsychological data to directly inform treatment in ED (Baldock and Tchanturia, 2007). The target population of CRT is mainly people with severe AN. People attending outpatient clinics are, in the main, able to benefit from more complex psychological therapies such as cognitive-behavioural therapy (CBT), psychodynamic therapy, family therapy or interpersonal therapy (IPT), etc. Nevertheless, neither of these interventions directly addresses the underlying process of thinking. In order to supplement the care of those receiving treatment in outpatients settings, Treasure and collaborators (Lopez *et al.*, 2008a, Lopez *et al.*, 2008d) have developed a personalised short intervention based on the principles of Motivational Interviewing and Motivational Enhancement Therapy (Miller and Rollnick, 2002, Miller *et al.*, 1992, Treasure and Schmidt, 2008), using a brief feedback intervention (DiClemente *et al.*, 2001, Schmidt *et al.*, 2006) as a lever for promoting change in the use of global processing strategies and in eating disorder symptoms.

### **9.2.1 Characteristics of feedback interventions**

Feedback has been utilised as part of psychological interventions for a long time but only in the last decade has become more relevant as a component of interventions targeted at several health problems and delivered through a number of different technologies (i.e. face to face, written, computerised, online or email, and mail feedback) (DiClemente *et al.*, 2001).

Providing generic or specific feedback to improve the effectiveness of interventions aimed at changing behaviours is a component of Motivational

Interviewing (Miller and Rollnick, 2002), and a core element of Motivational Enhancement Therapy (Miller et al., 1992). Miller and Rollnick argued that giving personalised feedback might enhance the motivation to change by broadening the discrepancy between the current status and the ideal situation. Also, motivational feedback is considered a non threatening method of increasing awareness about a risk or problem behaviour as it can be based on objective information drawn from test results (Emmons and Rollnick, 2001, Miller and Rollnick, 2002).

There is a wide range of types of interventions than can be grouped under the label of ‘feedback’. In order to generate a consensus over this matter, DiClemente *et al.* (DiClemente et al., 2001) provided a taxonomy and mechanisms of feedback which are presented in Table 9.1.

<b>Levels of generalisation of the feedback</b>		
<b>Generic</b>	<b>Targeted</b>	<b>Personalised</b>
Offers relevant information that is valid for the whole population to which the individual belongs	Adapts the information, which is still general, to a specific segment of the population for which the information is more relevant	Provides the most individualised feedback based on personal information or assessment
Subtypes: 1. Total population based 2. Subpopulation specific	Subtypes: 1. Based on demographic characteristics such as age or gender 2. Based on risk or other specific characteristic	Subtypes: 1. According to <b>source</b> of comparison: - <b>Normative</b> : compares individual’s information and a norm population - <b>Ipsative</b> : compares individual’s information at different points of time (longitudinal) 2. According to <b>content</b> : - Risk/problem information - Current status - Change options
e.g. connection between diet and risk behaviours	e.g. providing information about cognitive impairments related to ED	e.g. giving feedback on blood examination in comparison with healthy population ranges in patients with BN (current status normative feedback)

**Table 9.1 Types and mechanisms of feedback (DiClemente *et al.*, 2001)**

Apart from the categorisation described in the above table that refers to the level of generalisation of the feedback, feedback interventions can be categorised according to the level of assessment on which the feedback content is based. Thus feedback interventions may be not based on assessment (e.g. generic feedback) or they may be based on individualised assessment, which may last up to a few hours. It has been argued that taking part in an assessment would in itself be a mechanism that can promote change via the inherent feedback that the process involves (Bien *et al.*, 1993).

### 9.2.2 Brief Interventions

Feedback interventions may also vary in terms of the duration of the feedback (DiClemente *et al.*, 2001). Some feedback interventions are limited to brief advice (e.g. a 15-minute session providing information about risk factors for physical conditions associated with ED) whereas others may last several months (e.g. ipsative feedback on blood levels in patients with severe frequency of vomiting and laxative abuse). Interestingly, in two reviews of the impact of brief interventions in the area of alcohol related problems, it was found that well-designed brief interventions (most of them including feedback) promote more positive changes than no counselling and are comparable to longer and extensive treatments (Bien *et al.*, 1993, Moyer *et al.*, 2002). Similar results were found in a RCT that compared an extensive CBT treatment versus a Check-up intervention (including assessment, feedback with motivational and cognitive behavioural techniques) in marijuana users (e.g. Stephens *et al.*, 2000). Therefore brief interventions that involve feedback seem to be a cost-effective alternative for some behavioural problems.

In a through examination of the conditions that make brief interventions work, Miller and Sanchez (in Bien *et al.*, 1993) have highlighted the importance of **F**eedback as one of the 6 main elements for a successful brief intervention. Other elements are the individual's **R**esponsibility for change, clear **A**dvice on how to change, a **M**enu of change options, **E**mpathy, and reinforcement of **S**elf-efficacy, all of which are summarised by the acronym FRAMES.

### 9.2.3 Mechanism of Feedback

Feedback is generally based on facts resulting from an objective assessment. However, the intervention itself goes beyond this as it encourages the patient to make the feedback personally relevant and reflect on the implications of the information that is communicated to them (Emmons and Rollnick, 2001, Miller and Rollnick, 2002). Personalised feedback has been thought to improve motivation for taking up treatment and treatment retention (Davis *et al.*, 2003, Swanson *et al.*, 1999) as well as to contribute to a decrease in symptomatic behaviours e.g. in alcohol related problems (e.g. Bien *et al.*, 1993).

Although the mechanisms of feedback that help to produce change are still uncertain, there are a number of characteristics that have been posited as possible mechanisms of action. These mechanisms are present at some degree in most feedback interventions: motivational atmosphere, information or education about the individual's problems or risk, and/or how to overcome these problems/decreased risk, addressing attitudes or beliefs that might promote or prevent change, providing information or discussion about sources of support, providing normative information to compare the individual's current status, information about risk or protective factors, and highlighting the skills the individuals has or needs to develop in order to promote change (DiClemente *et al.*, 2001).

### 9.2.4 The use of feedback interventions in health care

In recent years, there has been a substantial increase in the interest for testing the impact of personalised feedback on change in health behaviours whereas earlier, the use of generic or targeted feedback was more common (DiClemente *et al.*, 2001, Rollnick *et al.*, 2008). Also, in the area of mental health there has been a widening of its use as part of Motivational Interviewing (Arkowitz *et al.*, 2008). In the field of ED, although Motivational Enhancement Therapy has been used for almost a decade with so far limited but promising results (Dean *et al.*, 2007, Feld *et al.*, 2001, Kaplan, 2002, Kotler *et al.*, 2003, Treasure *et al.*, 1999), the specific role of feedback as a single intervention has, to our knowledge, only been evaluated in one study (Schmidt *et al.*, 2006).

In the above study, the added effect of personalised normative and ipsative feedback to a guided CBT self-help treatment for BN and EDNOS on treatment up taking and outcome was evaluated in a randomised controlled trial (RCT). The feedback intervention included information about current psychological and physical conditions, risk factors, problems, and variables that promote or prevent change. Feedback was repeated during the intervention and delivered in different ways (e.g. motivational letters, computerised display of symptom status). Authors found that the group receiving feedback significantly reduced BN symptoms, particularly vomiting and dieting, after 6 months compared with the control group (patients with BN receiving treatment as usual without feedback). No advantages in the feedback group were found in terms of taking up treatment.

Taking into account the background given above, there is some evidence to propose that a brief intervention that includes motivational feedback might be useful in people with ED for promoting changes, both for life in general and in relationship to the illness. The intervention described in this chapter adds to the content of the feedback intervention used in Schmidt *et al.*'s study (2006), by incorporating personally relevant information about traits that *underlie* the ED phenotype.

### **9.3 The Intervention**

#### **9.3.1 Aims and rationale**

The overall aim of this feedback intervention was to identify, give feedback and create a formulation for addressing the information processing biases typically present in people with ED, i.e. weak coherence. Thus, the basic principle of this module is to translate the neuropsychological assessment into an individual formulation that encourages the patient to reflect on how and when this information processing bias manifests itself through their attitudes, thoughts, and behaviours in their daily life and how it relates to their illness.

### 9.3.2 Characteristics of the intervention

According to the taxonomy provided by DiClemente *et al.* (2001) the Brief Motivational Feedback Intervention could be categorised as a personalised normative feedback based on individual neuropsychological assessment of thinking styles, and particularly, the weak central coherence trait.

This intervention is delivered in three face-to-face sessions and was designed to be used in outpatient settings mainly as a part of the standard Maudsley model of treatment for AN following an initial psychiatric assessment. The rationale behind the development of this module is that people who develop an ED may exhibit the cognitive trait of weak central coherence both in neuropsychological testing and in relationship to food, weight and shape issues. Thus, this cognitive style may promote the grip of the psychopathology by narrowing the focus onto the details, rules, and the minutiae of laws of thermodynamics. It is possible that weak central coherence may underpin obsessive-compulsive personality traits that maintain (Schmidt and Treasure, 2006) the disorder and moderate the course of the illness (Anderluh *et al.*, 2008).

As AN and BN share the compulsive phenotype (Anderluh *et al.*, 2003, von Ranson *et al.*, 1999) as well as weak central coherence (see Chapters 4 and 5) this module is proposed to be a transdiagnostic tool for ED treatment.

### 9.3.3 The 3 sessions

The intervention consists of three sessions, each one with clear objectives and procedures. A description of these sessions is provided below:

#### **9.3.3.1 *Session 1: Neuropsychological Assessment***

The neuropsychological assessment of central coherence takes up to 30 minutes and it is carried out after the standard psychiatric assessment in a face-to-face session with a researcher. This assessment involves the use of a neuropsychological battery of tests consisting of three measures of local/global processing: the Rey-Osterrieth Complex Figure, the Embedded Figure Test and the Sentence Completion Task. A full description of these tasks is provided in Chapter 3.



Along with the neuropsychological evaluation, individuals taking part in this treatment module are also given a number of self-report questionnaires to complete regarding their cognitive style (see section 9.5.3).

If the patient shows sufficient evidence in favour of weak central coherence to merit the intervention (with a score 1 SD away from the norms of the healthy population scores on two or more tasks), they are given one session for feedback and formulation (50 minutes) and one session for review (60 minutes). Those with less extreme scores are given feedback only.

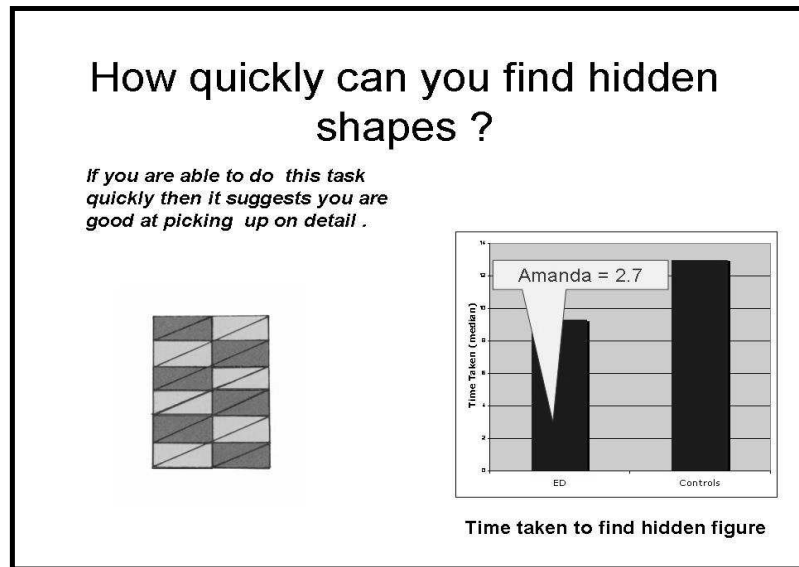
### **9.3.3.2 Session 2: Feedback and Formulation**

The objectives of session 2 are to provide a personalised feedback with regards to normal populations, to discuss how weak central coherence manifests in general life and in the ED, to develop an individual formulation, and to discuss behavioural experiments to counter these biases (Lopez *et al.*, 2008a).

#### Feedback

In this part of the intervention, the therapist provides feedback on the results of the neuropsychological assessment to the patient in a motivational, personalised and reflective style. The feedback is given in the form of printed charts where the score that the patient has obtained on the tasks and the scores of a healthy control population and of the general ED population on same tasks, are simultaneously displayed. These charts also contain information about the meaning of the neuropsychological results. Therapist and patient jointly explore the results to ensure that the patient understands the meaning and implications of the test results. Figure 9.1 shows an example of the charts used in the feedback session, displaying results from the Embedded Figure Test of a fictitious patient (Amanda).

**Figure 9.1 Example of feedback charts for EFT**



### Formulation

The formulation stage includes a discussion of the role that extreme performance, characterised by a tendency towards either of these traits (weak central coherence or cognitive inflexibility) plays in different domains of the patient's life, i.e. academic life, career, family life, close and social relationships, and how this may have evolved and shaped the life course. The origins of these thinking styles are also explored e.g. who else in the family has these trait, were they present before the onset of the eating disorder, etc. Finally, the focus of the discussion is on how these traits underpin and shape eating disorder symptoms.

### ***9.3.3.3 Session 3: Reflection and Transcending Targets***

This last session brings together the contents of session 2 with the aim of reflecting further on the developed formulation and translating the reflection into steps towards change.

## Reflection

This part of the final session is aimed at reviewing and reflecting on the formulation developed in the previous session. The therapist explores the ecological validity of the discussed formulation beyond the difficulties related to the eating disorder.

## Transcending Targets: overcoming the detail bias

The final part of this module aims to examine how the patient can manage to strike a balance in their behaviour by moving to a less extreme position or developing strategies to enable them to transcend their usual biases.

With regards to the detail bias (weak central coherence), patients are encouraged to adopt a more integrative approach by stepping back from the detail so as to be able to see the whole. This involves monitoring how they exhibit this behaviour in everyday life and considering the advice of others who are more able to see the 'bigger picture' in order to model their spontaneous approach. Also, the therapist encourages the exercise of global enhancing strategies, such as the use of images, diagrams, headings, bullet points, mind maps, etc., which can help patients to keep the focus away from detail. Patients are asked to try to introduce and practice zooming out to the 'bigger picture' of everyday life in relation to general activities and eating disorder prompts and behaviours.

Some patients exhibit a cognitive style characterised by an imbalance between extreme speed and accuracy. Patients who choose to make no mistakes at the cost of slowness in tasks (e.g. EFT) are encouraged to make a judgement about this balance and set reasonable limits.

Behavioural experiments are designed and discussed in the session in which patients are encouraged to challenge their typical cognitive style and try them out the session. Also, the therapist and patient discuss difficulties and strategies to overcome obstacles that might arise in the course of the experiments and problem solving strategies are taught that can help overcome any foreseen difficulties. The patient is also given a worksheet that summarises the general meaning of the assessment and suggests follow-up strategies.

The feedback intervention forms one component of the Maudsley Model of treatment for ED that address perfectionism and obsessive-compulsive personality traits. Other components of the treatment (anxiety/emotional avoidance,

interpersonal relationships and pro-ED beliefs) have to be assessed and addressed. Generally, further treatment is considered. Then, a summary of the intervention is passed on to the therapist assigned to continue the treatment and who will then integrate these results into the standard Maudsley model of individual outpatient care.

## **9.4 Aims and Hypothesis of the Study**

The main aim of this pilot study was to contribute to the development of a brief intervention for people with eating disorders addressing weak central coherence, and to explore its acceptability and effectiveness in terms of helping patients to transcend the bias towards detail.

The proposed brief intervention was designed by Professor Treasure based on neuropsychological studies carried out in the Eating Disorders Research Unit, with the purpose of helping patients to recognise and overcome their bias for a characteristic cognitive style and its influence on their illness and general functioning. The hypotheses were that a brief intervention focused on giving feedback about patient's strengths and weaknesses in information processing, comparing these with population norms, and formulating how this cognitive style may impact on other domains of functioning (1) would improve the patient's awareness of their predominant cognitive style, (2) teach them how to transcend the bias towards detail when needed and appropriate, and (3) would be of value as part of the standard treatment for outpatients with ED.

## **9.5 Methods**

### **9.5.1 Design**

This study used an observational prospective consecutive case series design. No control group was utilised.

### 9.5.2 Participants

Ten consecutive referrals to a National Specialist Eating Disorders Unit (outpatient) at Guy's Hospital between May and October 2004 were invited to take part in this study. All participants first completed a standard psychiatric assessment. Then, all had a neuropsychological assessment.

In order to be included in the feedback intervention, subjects had to show 'extreme performance' in at least two of the variables measured through the neuropsychological tasks assessing a bias toward detail and global processing difficulties. An 'extreme performance' was defined as obtaining scores:

- Below 1 standard deviation (SD) on coherence indices of RCFT in comparison with the results obtained by a healthy control group reported in this thesis in Chapters 4 through 6 (normally distributed data)
- Below the lower quartile (percentile 25) in time and errors in the EFT in comparison with the results obtained by a healthy control group reported in this thesis (non-normally distributed data)
- Above the upper quartile (percentile 75) in the total score on the SCT in comparison with the results obtained by a healthy control group reported in this thesis (non-normally distributed data).

Consequently, patients ( $n = 2$ , 10%) who had 'extreme performance' in only one or none of the aforementioned variables were excluded from the intervention and only a brief feedback was provided before their treatment continued as usual.

Eight cases fulfilled the inclusion criteria for the complete intervention: (1) to have an ED (AN, BN or eating disorder not otherwise specified, EDNOS) as defined in the DSM-IV (APA, 1994), (2) to be able to be treated in outpatient settings (e.g. not having high psychological and physical risk), (3), to show extreme indices of weak central coherence according to the neuropsychological assessment, and (4) to have given consent to take part in this study. Exclusion criteria included: severe mental illness such as psychosis; acute suicidality; substance dependence; severe physical co-morbidity such as diabetes; pregnancy; learning disability or inability to understand English to a level that precluded the use of feedback.

One case dropped-out after the intervention and did not complete the follow-up assessment. This was a patient who expressed a lack of motivation to receive treatment. A total of 7 cases completed all the assessments.

### 9.5.3 Measures

All patients were clinically assessed by an experienced and trained clinician (JT) who assigned diagnoses using a semi-structured clinical interview for DSM-IV diagnosis which has been developed, validated, and routinely used in our Unit.

The neuropsychological battery of tests administered to examine the eligibility of the patients consisted of the following measures of coherence: *The Rey-Osterrieth Complex Figure- copy and recall form* (RCFT; Osterrieth, 1944), the *Embedded Figures Test* (Witkin et al., 1971), and the *Sentence Completion Task* (SCT) (Happé et al., 2001). These tests have been shown to be sensitive in previous studies in ED samples. A full description of these tests is provided in Chapter 3. The National Adult Reading Test was also administered to all participants as an estimate of intellectual ability (NART; Nelson and Willison, 1991).

Two self-report questionnaires were administered to all patients at baseline:

*Cognitive Flexibility Scale* (Martin and Rubin, 1995) This is a valid self-report scale consisting of 12 items (6-point scale) constructed to measure the individual's perception with regards to their cognitive flexibility. This measure was chosen to evaluate the perception of change in this ability after the intervention.

*Cognitive Styles in Action* (Treasure & Lopez, 2006, unpublished). This is a 25-item self-report questionnaire constructed to measure the individual's perception of their cognitive styles and ability to switch between a predominant focus on detail versus a global style according to environmental demands (see Appendix E). It is composed of four subscales: *Cognitive Style* (maximum score = 24) which measures to which degree the individual identifies him/herself as having a tendency for global (higher scores) or detail (lower scores) cognitive processing; *Perfectionism* (maximum score = 42) which measures to what extent the individual attributes perfectionist tendencies to themselves (higher scores mean stronger perfectionism); *Importance* (maximum scores = 36) which measures to which degree the individual values the ability to process information globally versus focus on detail and cognitive flexibility (higher scores mean greater value); and *Confidence* (maximum score = 48) which examines whether the individual feels able to respond to tasks or demands where global thinking is required (higher scores mean more confidence). This was an explorative novel instrument that was created for this study.

After the intervention, BMI was measured and the self-report questionnaires were repeated.

Finally, two months after the post-intervention assessment, patients were re-evaluated using the self-report questionnaires and BMI was taken, and a *Satisfaction with the intervention feedback form* was added to the evaluation measuring the degree of satisfaction with different aspects of the treatment. This questionnaire consisted of 5 items rated by means of a visual analogue scale (VAS). Scores ranged from 0 to 10 where 0 means not satisfied at all and 10 means extremely satisfied. A brief written comment could also be included at the patient's choice. The questionnaire contained the following questions (words in brackets correspond to the label on Figure 9.4):

- How positive do you feel about the intervention you have received? (Positive)
- How effective did you find the intervention? (Effective)
- Do you feel that the intervention provided you with a better understanding of your cognitive style? (Understanding)
- Do you feel that the intervention provided a better understanding about how your cognitive style relates to your real life? (Real life)
- How useful did you find the intervention in terms of translating the content into practical skills/strategies to your real life? (Translate)

Neuropsychological function was not re-assessed after the baseline assessment because the time between the pre and post-intervention evaluation was short (less than a month) and tasks which might have given relevant information with regards to the effectiveness of the intervention (improvements in global processing, such as RCFT and SCT) would be subject to practice effects. Validated alternative forms were not available at the time of these assessments.

#### 9.5.4 Procedure

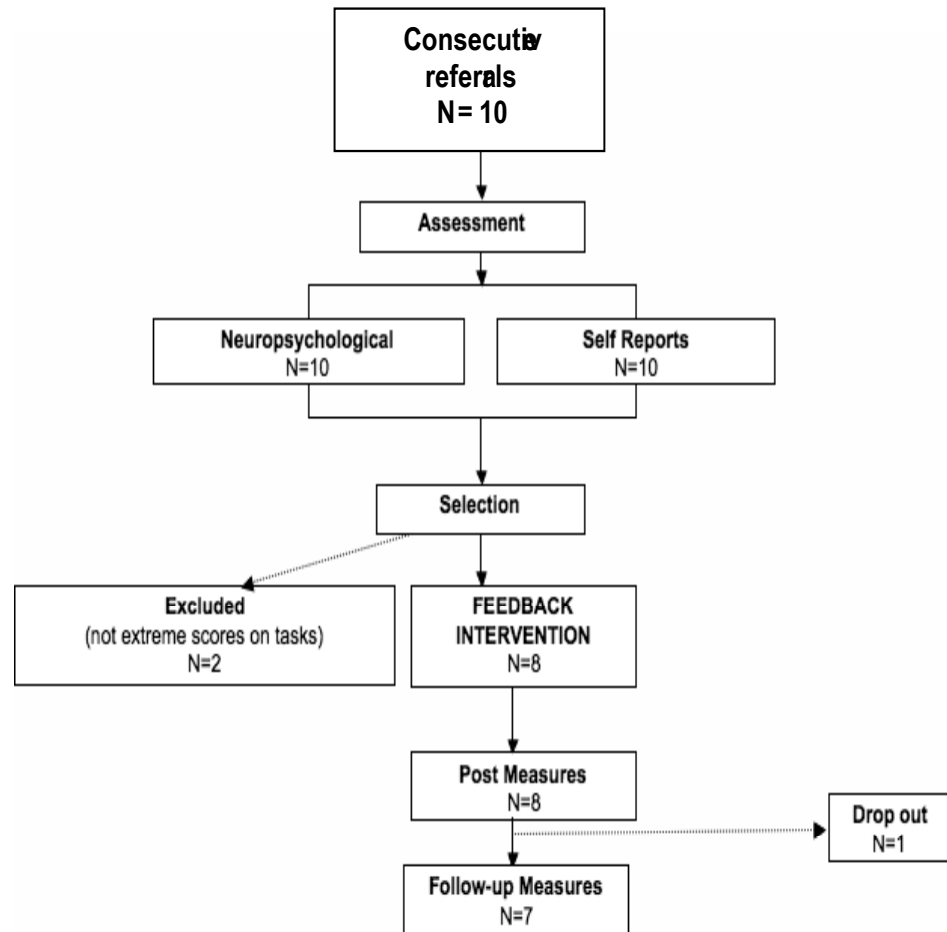
The procedures of this study were approved by the Institute of Psychiatry/South London and Maudsley NHS Trust Research Ethical Committee (Study number 020/05). Written informed consent was obtained from each participant before participation in this study. Confidentiality of participants was

assured at all stages. Participants were allowed to withdraw from the study at any time.

All patients were offered an individual neuropsychological assessment after the first standard psychiatric assessment, provided that they were free of risk and psychopathological conditions described in the exclusion criteria, and before commencing the standard Maudsley model of individual outpatient treatment. After the neuropsychological assessment, patients who did not present an extreme bias in neuropsychological tasks were invited to a session in which a brief feedback based on the neuropsychological exploration was given and they then continued with the standard treatment. Those who fulfilled the inclusion criteria were invited to continue with the brief motivational feedback intervention. The whole intervention was provided within a month from the first standard psychiatric assessment and after the third session patients were re-evaluated with the self-report questionnaires.

A researcher (CL) conducted the assessment and prepared the materials for feedback. Feedback, reflection and formulation sessions were delivered by Prof. Treasure. Figure 9.2 shows the procedure followed in this pilot study.





**Figure 9.2 Feedback intervention flow chart**

#### 9.5.5 Data analysis

Analyses were conducted using SPSS Version 16. In order to detect whether the intervention had an impact on the variables measured by the Cognitive Flexibility and Thinking Styles in Action self-report questionnaire, data resulting from the baseline, post-intervention and follow-up assessments were compared using one-way ANOVA for repeated measures. Changes on BMI were analysed using the same statistical procedure. The nominal significance level was chosen to be .05. Partial eta squared was calculated as a measure of effect size. A measure of acceptability (*Satisfaction with the feedback intervention form*), which involves visual analogue scales (VAS), was analysed using descriptive statistics only.

## 9.6 Results

### 9.6.1 Demographic and Clinical Characteristics

Ten patients with ED were initially invited to take part. Their diagnoses were as follows: seven had restricting AN, one had binge-purge AN, one had EDNOS and one had binge-eating disorder (BED). Two patients (20%) with restricting AN were excluded from the intervention as they did not have extreme scores on central coherence. Therefore, only 8 patients were involved in the intervention and their data are presented below. No drop-outs during the intervention were observed but one patient withdrew from the study after the post-intervention assessment.

From the eligible participants, 7 were Caucasian British females and one was Caucasian American. Their mean age was 28.6 years ( $SD = 12.8$ , range = 16-53), the mean age of onset was 15.5 years ( $SD = 2.5$ , range = 12 - 19), and a mean estimate of intellectual ability of 113.9 ( $SD = 7.0$ , range = 105-125).

BMI's means ( $M$ ) and standard deviations ( $SD$ ) for AN participants are presented in Table 9.2 along with BMI for the only cases with EDNOS and BED, at the three points of assessment.

**Table 9.2 Patients' BMI at pre, post and follow-up**

<b>BMI</b>	<b><i>N</i></b>	<b>Baseline</b>	<b>Post- Intervention</b>	<b>Follow-up</b>
AN patients	6 (5 at follow-up)	15.9 (.94)	17.5 (1.8)	17.9 (3.0)
EDNOS patient	1	24.50	24.54	24.00
BED patient	1	40.10	37.2	35.99

AN= anorexia nervosa, EDNOS= eating disorders not otherwise specified, BED= binge-eating disorders. Means ( $M$ ) and standard deviations ( $SD$ ) are presented.

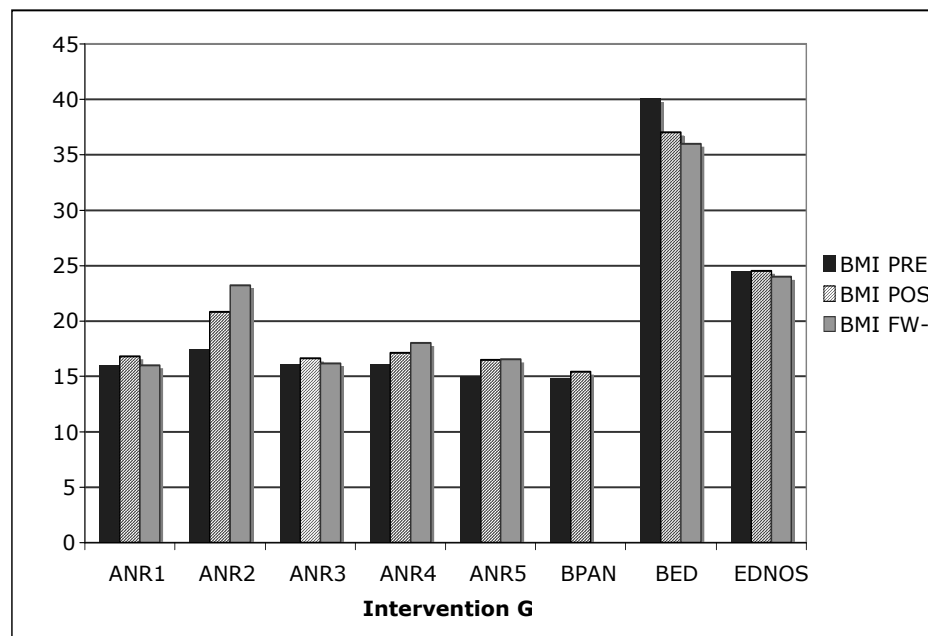
A one-way repeated measure ANOVA was conducted to compare the BMI of AN patients at baseline (before the intervention), post intervention (immediately after the reflection session) and at follow-up (2-month after the intervention). There

was a trend of a statistically significant effect for time with a large effect size (Wilk's Lambda = .15,  $F_{(2,3)} = 8.4$ ,  $p = .06$ , multivariate partial eta squared = .85).

Individual change patterns in BMI are displayed in Figure 9.3.

In general, increases in BMI were observed in women with AN, the woman with BED reduced in BMI and the woman with EDNOS maintained her BMI over the course of the intervention. The only patient with binge-purge AN did not complete the follow-up assessment.

**Figure 9.3 Individual's BMI at the three assessment points**



ANR = Restricting Anorexia Nervosa, BPAN = Binge-purge Anorexia Nervosa, BED = Binge-eating Disorders, EDNOS = Eating Disorders Not Otherwise Specified, BMI = Body Mass Index, PRE= Previous to the intervention, POST = After the Intervention, FW -UP = 2-month follow up

### 9.6.2 Neuropsychological Function

Results of the neuropsychological function of the 8 women who took part in the intervention are shown in Table 9.3 along with the results of a healthy control group (data from previous chapters are provided as a reference only). It is possible to appreciate that the intervention group was extreme on most of the scores as was required in order to participate in the intervention. Thus, most of the women in this

group obtained lower central coherence indices in the RCFT, failed to process information globally in the verbal domain (SCT) and about a half excelled in speed of completion of the EFT.

As a whole, the results below demonstrate greater global processing difficulties and a somewhat advantageous detail processing style.

**Table 9.3 Neuropsychological profiles of participants in the pilot study**

	Intervention Group <i>n</i> = 8	Healthy Controls <i>n</i> = 42 *	% of individuals with extreme scores
RCFT Coherence Index <sup>a</sup>	1.0 (.45)	1.6 (.30)	75 %
EFT time <sup>b</sup>	8.3 (4.6-18.1)	12.2 (7.9-15.3)	50 %
EFT time out failures <sup>b</sup>	1 (0-2)	1 (0-2)	38 %
SCT <sup>b</sup>	3 (2-5.7)	0 (0-1)	88 %

RCFT = Rey-Osterrieth Figure Test, EFT = Embedded Figures Test, SCT = Sentences Completion Task

<sup>a</sup> = Data normally distributed (means and standard deviations are shown)

<sup>b</sup> = Data non-normally distributed (medians and upper and lower quartiles displayed)

\* = Results obtained by a healthy control (HC) group are given as reference

### 9.6.3 Patients' evaluation of their cognitive style: Cognitive Flexibility and Cognitive Styles in Action

One-way repeated measures ANOVAs were conducted to compare scores on the Cognitive Flexibility Scale and subscales on Cognitive Styles in Action Questionnaire at baseline, post intervention and follow-up. The means (M) and standard deviations (SD) are presented in Table 9.4.

Moderate effect sizes were found for the effect of time in improvements on the Cognitive Flexibility Scale although this did not reach statistical significance due to low power (Wilk's Lambda = .53,  $F_{(2,6)} = 2.7$ ,  $p = .15$ , multivariate partial eta squared = .47). On the Cognitive Styles in Action, no changes over time were found

in the perception of what type of cognitive style was predominant (Wilk's Lambda = .49,  $F_{(2,5)} = 2.6$ ,  $p = .17$ , partial eta squared = .51) nor on the Importance Scale (Wilk's Lambda = .88,  $F_{(2,5)} = .35$ ,  $p = .72$ , partial eta squared = .12). On the other two scales of the Cognitive Styles in Action questionnaire, a trend for significant effects of time were found in the reduction of perfectionism with a moderate effect size (Wilk's Lambda = .39,  $F_{(2,5)} = 3.8$ ,  $p = .09$ , partial eta squared = .61) and the level of confidence in using global strategies and thinking with more flexibility when required was increased with a moderate effect size as well (Wilk's Lambda = .25,  $F_{(2,5)} = 7.5$ ,  $p = .03$ , partial eta squared = .75).

**Table 9.4 One-way repeated measures ANOVA for self-reports on thinking styles**

Scale	Baseline <i>n</i> = 8	Post- Intervention <i>n</i> = 8	Follow-up <i>n</i> = 7	$F_{(2,6)}$	<i>p</i>	Eta squared
Cognitive Flexibility Scale	46.4 (7.8)	50.3 (12.3)	51.8 (11.9)	2.66	.15	.47
Cognitive Style *	9.6 (2.8)	7.5 (1.6)	8.6 (2.9)	2.57	.17	.51
Perfectionism *	25.6 (3.2)	22.3 (3.7)	22.00 (6.4)	3.82	.09	.61
Importance *	26.1 (3.2)	26.6 (5.2)	27.6 (2.8)	0.35	.72	.12
Confidence *	25.7 (4.2)	26.0 (7.3)	29.4 (7.6)	7.54	<b>.03</b>	<b>.75</b>

\* Cognitive Styles in Action Subscales

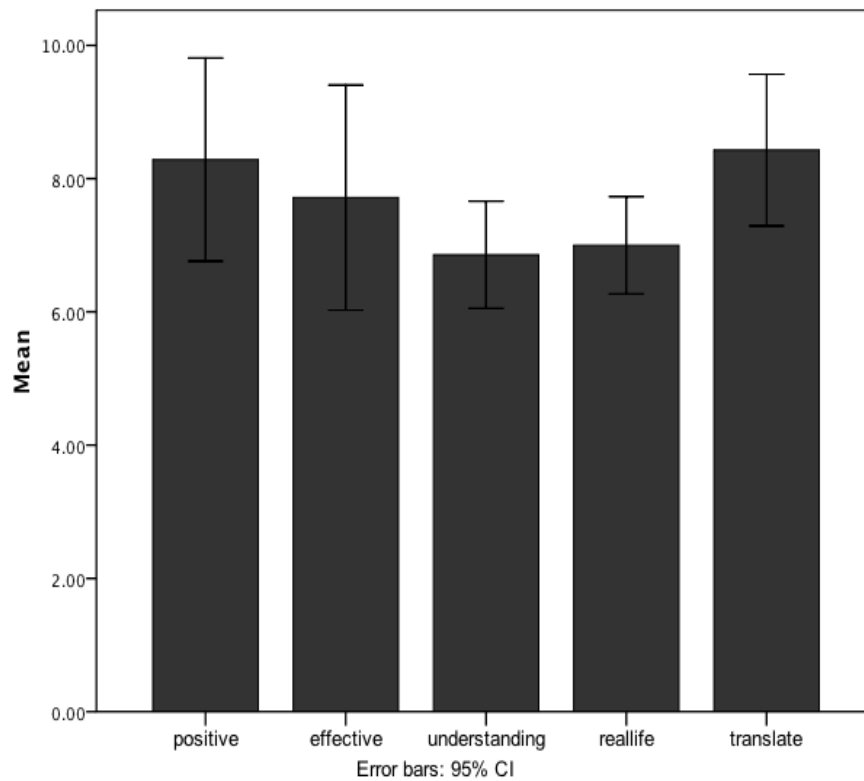
There were no relationships between BMI and scores on the self-report variables. Reductions on the Perfectionism subscale were found to be correlated with the increase on the Confidence subscale of the Cognitive Styles in Action questionnaire ( $r = .77$ ,  $p = .04$ ).

#### 9.6.4 Satisfaction with the treatment

Results on the different aspects evaluated in the *Satisfaction with the treatment questionnaire* were summarised with mean scores given to each scale per participant. There were no scores below 4 on any of the scales given by any of the participants.

Figure 9.4 displays the mean scores obtained from the *Satisfaction with the feedback intervention form*.

**Figure 9.4 Mean scores in dimensions of satisfaction with the treatment ( $n = 7$ )**



No relationships were found between improvements in perfectionism or confidence scales of the self-report (found to be the aspects that showed more change following the intervention) and any dimension of satisfaction with the treatment.

In addition, most of the patients wrote comments on the satisfaction form pointing out some helpful aspects of the intervention. The quotes below were indicative of most of these comments:

- ‘The feedback intervention helped me to understand how I have a strong tendency to focus in details but how I can also see the bigger picture if I make an effort’
- ‘It gave me understanding of my usual cognitive style and highlighted areas where I might try a different more effective strategy’

- ‘I found myself to be able to zoom in and out of looking at the bigger picture and at the detail and reflect about which one is better for me to focus on at a precise moment’
- ‘I found it useful looking at the data and how I was related to other participants and also discussing practical applicable ways to use what I have learned’
- ‘I valued the opportunity to talk about how I felt, make progress and to be offered comments on cognitive styles from someone I respect’.

A few comments about how the intervention might be improved were also received:

- ‘I needed help to see particular ways in which I can use this to help me’
- ‘I don’t understand examples of when I need to see the bigger picture and how to do it’
- ‘I thought it was helpful but some of the terminology was difficult to understand’
- ‘I would need more time working with someone in order to understand it more’

Finally, patients were asked to write some reflections about whether this brief intervention had any impact on their real life after six months following the intervention. This feedback from patients was informative and helped to develop the intervention further. The following excerpt was taken from one of the patients who took part in this study and illustrates the effect of the intervention beyond the ED.

*“Understanding my cognitive style has had a positive impact on my life. Firstly, it has identified the thinking styles that have contributed towards the anorexia nervosa. Secondly, the results provide a basis for targets/experiments to help change the undesirable thinking patterns, and enable me to improve my quality of life.*

*An understanding that I have an analytical/detail focus has helped me to set targets for reducing this with food. For example, I used to be very preoccupied with counting the calories in food. By realising that this is due to my analytical thinking, I have taken steps to stop weighing food, to start eating food such as fruit without*

*labelling...and I generally no longer look at the number of calories in food or count calories for the day.*

*My focus on the detail of food, and disregard for my wider life, had also made it difficult to see how gaining weight would lead to a better life. However by producing a display booklet picturing my hopes for 'my life after anorexia' I can continually remind myself of the bigger picture, and what I can have in life once I can maintain a healthy weight.*

*Since receiving the feedback from the assessment I have been more aware of how my cognitive style plays a role in my life [...] This has helped me to understand why I take great care over tasks, both at home and in my work, to ensure that they are carried out to the highest standard, with few flaws or errors. While this trait can be useful [...] it slows down progress in others, resulting in my tendency to work for as long as it takes until a task is completed to perfection. [...] understand the conflict between my focus on detail and ability to see the bigger picture [...] explains why I am overcome with indecision when selecting food in the supermarket – I have a conflict between focusing on the nutritional information and striving for better nutritional health.”*

## **9.7 Discussion**

The aim of this study was to develop a brief module of intervention focused on cognitive styles for outpatients with ED, as part of the treatment package based on the new Maudsley maintenance model for ED (Schmidt and Treasure, 2006). Particularly, this small pilot study examined preliminary findings about acceptability and perceived effectiveness of the intervention.

The hypotheses that the intervention would be of value for patients and would make patients aware of their cognitive styles and how to transcend the bias for detail were supported by the results. Thus, overall the brief motivational feedback intervention was found to be acceptable by the patients and highly valued as shown by their positive comments and scores given to the different aspects of satisfaction with the module. Also, self-report measures showed that it helped to improve confidence in flexibly balancing the detail focused and global strategies according to environmental demands. Although other aspects measured by self-reports, such as



cognitive flexibility and perfectionism, moved towards the desired, hypothesised direction following the intervention, these changes were not statistically significant. Moderate effect sizes were, however, found which suggests that the lack of statistical differences might be due to the small sample size in this pilot exploratory study.

There were two aspects that did not change at all on the self-reports measures: how patients would define their predominant cognitive style (results are shifted towards the detail focused end of the scale) and the importance attributable to both the ability of being flexible and that of thinking and seeing the 'bigger picture'. These results were expected as the intervention did not intend to firstly, change patients' predominant thinking style but rather was aimed at helping them to start to overcome the bias toward detail, and secondly, not to push patients to give more importance to global processing and flexibility but rather to use cognitive strategies in a more balanced manner and adjust them according to specific demands.

Finally, this study provides data about the number of patients attending an outpatient clinic who might benefit from an intervention targeting cognitive styles. Eighty percent of the originally invited patients for this study showed signs of weak central coherence whereas the other 20% performed as well as healthy controls. Similarly, around 70% of a sample of 42 participants with ED in a later study had impaired scores on the RCFT (Roberts, personal communication). Additionally, it was interesting that patients presented the weak coherence profile irrespective of their main ED diagnosis (BED and EDNOS were included) which indicates that the intervention might be a useful transdiagnostic tool.

Three aspects of the intervention appear to be important and merit emphasis and inclusion within novel strategies in the treatment of ED. Firstly, providing feedback to patients on test results is a core element that helps to promote change in the motivational interviewing model (DiClemente *et al.*, 2001, Miller and Rollnick, 2002) and has been successfully used in the treatment of BN and EDNOS in which it was found to be associated with better outcomes in treatment (Schmidt *et al.*, 2006). Therefore, this study adds some evidence in favour of using feedback as an integral part of the treatment of ED. The tone of the feedback intervention is not judgemental which enables patients to collaborate with the therapist and reflect without resistance on how characteristics of patients' functioning relate to the ED psychopathology. Secondly, targeting cognitive styles that constitute underlying traits in ED and as such may not be evident to the patients themselves (Gottesman and Gould, 2003),

may help them to moderate these extreme dispositions and improve coping strategies (Treasure *et al.*, 2007a) increasing the sense of control and self-efficacy and channelling them in favour of recovery and general functioning. Other characteristics typically found in ED patients, such as emotional avoidance, warrant the provision of interventions that have a cognitive rather than emotional emphasis as part of treatment. Thirdly, brief interventions that target specific features that maintain psychiatric disorders as opposed to broad, more general interventions have been shown to be useful and valued as adds-on to standard treatment. For example, in obsessive-compulsive disorders a brief cognitive remediation intervention to enhance global processing strategies was found to be successful for both healthy controls and patients (Buhlmann *et al.*, 2006). The observations obtained from the above studies together with the present pilot study add support for further development and research on brief modules of intervention, as part of standard treatment, that address specific aspects in the development and maintenance of ED and can be chosen on the basis of individualised assessments.

It remains a challenge that requires further exploration to establish how this feedback intervention compares with longer modules, such as, for example, CRT

#### Limitations of the study

A number of methodological limitations may be mentioned for this study. Firstly, this pilot study lacked a control condition and a control group therefore the changes found after the intervention cannot be attributable to the intervention only. For example it might be useful to use an A-B multiple baseline design which is a type of design suitable for case series studies and where the effect of the intervention is evaluated by examining changes across different baselines. Thus, it would be possible to identify whether changes detected in a study like this appear only when the intervention is introduced (Hersen and Bariow, 1976).

Secondly, one of the self-report measures was a tool that was still being developed and fine-tuned, therefore results obtained from it may not be generalisable as the measure has yet to be validated. Parts of this questionnaire have been incorporated into a new measure that is aimed at capturing cognitive flexibility and central coherence and has been validated with an ED population (Roberts *et al.*, in preparation).

Thirdly, although it was not the objective of this intervention, it would have been interesting to report changes in the neuropsychological profile after the intervention. In order to do this, some of the measures utilised, such as central coherence indices of the Rey-Osterrieth Complex Figure (RCFT) and the Sentence Completion Test, would need to have a validated alternative form. One possibility is the utilization of Fragmented Pictures Tests to measure improvements in global processing (Snodgrass and Corwin, 1988, Snodgrass *et al.*, 1987) as mentioned before, as there is a wide availability of pictures with measured levels of difficulty from where alternative and equivalent versions of the task can be created. This task has been pilot in people with ED by members of our research Unit with promising results.

Finally, this was a pilot study that was aimed at contributing to the development of a new intervention for ED based on neuropsychological assessments. Some changes were noticed and effect sizes were moderate, however, the insufficient power of the sample precluded the identification of significant differences within subjects pre and post the intervention, and at follow-up assessment. Randomised Controlled studies with bigger sample sizes that include valid clinical and neuropsychological measures would help to better understand the effect of feedback on both ED outcome (e.g. reduction of ED psychopathological features) and neuropsychological performance.

### Strengths

Although a small study, this work has contributed to the development of the feedback intervention into its current form, as described at the beginning of the chapter. Patients found it acceptable and informative. The only drop-out from the study occurred after the intervention before the follow-up assessment, which is a good index of acceptability in comparison with the usual rates of drop-outs from treatment (Halmi *et al.*, 2005b). Acceptability was also reflected in the qualitative feedback provided by patients. Patients were able to introduce ‘bigger picture thinking’ in their daily activities and relate the excessive attention to detail to both the development and maintenance of the illness, as illustrated in patients’ feedback (Lopez *et al.*, 2008a, Lopez *et al.*, 2008d). The study identified elements that need to be taken into account when translating neuroscience findings related to central coherence into clinical practice. For example, although people with ED tend in

general to present a cognitive style compatible with the weak central coherence hypothesis, not all patients with ED may require the intervention as across individuals and domains differences in the distribution of this trait have been found (see Chapter 7). These results indicate that a preliminary assessment may be needed to target treatment for each patient. Finally, patients also mentioned that they would need more guidance to be able to transfer what they have learnt in sessions to the real life. Therefore, it might be possible and helpful that after the intervention, a follow-up 'booster' session will be implemented or that this information will be accessible to the clinicians and professionals who will provide therapy after this brief intervention so they can include it into the broader treatment. Also, providing worksheets with more information about strategies for overcoming the detail bias or supporting the work between sessions with a workbook designed to reinforce the concepts involved in the intervention might help patients to get more benefits from the intervention.

## **9.8 Conclusion**

The pilot study presented above was a preliminary effort to translate laboratory-based evidence from neuropsychological studies into a brief, motivational feedback intervention suitable for out-patient settings within a broader standard treatment or stand alone intervention in specific cases (Lopez *et al.*, 2008a). The feedback intervention demonstrated acceptability and was found to be of value for people suffering from an eating disorder and interestingly this seemed to be irrespective of their diagnostic category. Overall, these results suggest that the neuropsychological assessment, personalised feedback and formulation intervention is acceptable and is associated with some positive changes in terms of reduction of perfectionism (core obsessive-compulsive personality trait), improvements in BMI, and increased confidence in more adaptively adjusting the application of cognitive skills. These changes, together with the encouraging feedback of patients about the effectiveness of the intervention, set the basis for further research on this type of intervention for ED. Finally, this module fits well within the new Maudsley model of treatment for out-patient settings due to its assessment-based screening, short nature and its specific objective.

Taking all the above together, a short motivational feedback intervention seems a promising approach to targeting extreme cognitive styles in ED, one of the factors thought to play a role in the maintenance of the disorder (Treasure, 2007, Treasure *et al.*, 2005a). There are, however, a number of uncertainties as to whether the brief feedback promotes transference of skills to real life, leads to changes in neuropsychological performance, how it interacts with other aspects of the treatment, and more importantly, if it has a positive effect on treatment outcomes related to the ED psychopathology.

Future developments of this study may include cognitive performance assessment after the intervention with alternative and validated instruments to avoid learning effects (Szoke *et al.*, 2008). Also, investigating innovative technologies such as computerised assessment and feedback, which are being tested in treatment for other behavioural problems, might make this approach more cost-effective (e.g. Gilbert *et al.*, 2008, Moreira and Foxcroft, 2008, Walker *et al.*, 2007). Such an assessment may also include other features relevant for the maintenance of ED such as set-shifting difficulties (Treasure *et al.*, 2007a). The need for a therapist to provide feedback and make the intervention personally relevant needs to be studied further. It might be possible that due to the severity of ED, patients would need more interpersonal assistance than in other behavioural problems (DiClemente *et al.*, 2001). Finally, addressing some of the aforementioned uncertainties with regards to the effectiveness of this feedback intervention it will make it possible to better understand the mechanisms whereby feedback produces changes and when and how it needs to be included in the ED treatment.

## **10 GENERAL CONCLUSIONS: ACHIEVING COHERENCE**

### **10.1 Introduction**

The overall aim of this thesis was to advance the understanding of anomalies in the cognitive functioning of individuals suffering from an ED that may act as vulnerability factors for the development and maintenance of the illness. In particular, the focus of the thesis was placed on a newly explored cognitive feature in ED namely ‘weak central coherence’: a bias in the cognitive style towards detail-focused processing accompanied by difficulties in global, integrative processing of information (Frith, 1989, Happé and Booth, 2008).

In order to achieve the overall aim, two main objectives were pursued.

The first objective was to examine the concept of weak central coherence under the umbrella of the endophenotype approach. The second objective was to explore how findings from neuropsychological studies can be translated into clinical interventions and incorporated into the treatment for ED.

The methods proposed to attain these two objectives, the conclusions reached within this thesis, and the recommendations for future development and research in the areas pertaining to these two objectives, are described below. Implications of the findings of this thesis for the understanding of central coherence in people with ED are examined. Finally, a summary of limitations and contributions of this thesis are discussed.

### **10.2 An Examination of the Concept of Central Coherence in the Eating Disorder Population: An Endophenotype Approach**

In order to achieve this first objective, the two first criteria for an endophenotype in psychiatry were explored using a cross-sectional study design and a quantitative analysis of data. Firstly, the association of weak central coherence with the illness in the population (criterion 1) was examined by administering a battery of tests including tasks tapping aspects of central coherence, in both verbal and visual domains, to women currently fulfilling the DSM-IV criteria for the main ED

diagnostic categories i.e. anorexia nervosa (AN) and bulimia nervosa (BN). Forty-two women with AN, forty-two with BN and forty-two healthy women (healthy control group, HC) took part in these studies (Chapters 4 and 5). Secondly, the same battery of tests was utilised in a study involving forty-two women that have reached full recovery after a period of acute AN or BN (EDRec), and their results were compared with the results obtained by the HC that took part in the two aforementioned studies (Chapter 6). All groups were equivalent in age and intellectual ability.

The full central coherence battery of tests consisted of the Un/segmented Block Design Test (Un/Seg BD) and the Embedded Figures Tests (EFT) as measures of efficient local processing and the Rey-Osterrieth Complex Figure Test (RCFT), the Homograph Reading Task (HRT) and the Sentence Completion Task (SCT) as measures of adaptive global strategies. This neuropsychological battery was accompanied by a series of self-report measures of co-morbid conditions (the Hospital Anxiety and Depression Scale – HADS - and the Obsessive-Compulsive Inventory - OCI-R) and a measure for screening for autistic-like traits (the Autism-Spectrum Quotient - AQ). All participants were interviewed to establish ED lifetime and current diagnosis with the EATATE semi-structured interview. Effects of age, level of intellectual ability, duration of illness and co-morbid conditions on processing style were examined.

The hypothesis that central coherence as measured by the aforementioned tasks was going to be weaker in women with *lifetime* ED (current AN, BN and recovered) relative to the HC group, was confirmed by the studies carried out in this thesis (Chapters 4 through 6). Overall, the results demonstrated that in general, women with lifetime ED had more difficulties in global processing tasks in both visual and verbal modalities and tended to be superior in local (detail-focused) processing in visual processing tasks in comparison with the HC group. These findings are in line with the little previous evidence in favour of a superior local processing in ED (Southgate, 2005, Southgate *et al.*, 2007, Tokley and Kemps, 2007) and the more extensive evidence in favour of difficulties in integrative processing in ED (for a systematic review, see Chapter 2).

Between-group comparisons showed that differences between HC and lifetime ED groups were found in three of the five central coherence tasks in the AN study, and four of the five in the BN and EDRec studies. The HRT and Un/seg BD

were in the main the least sensitive tasks to detect differences between groups. For example, no differences in the HRT were found in AN and only a statistical trend was found in EDRec, and no differences were found in the benefit from segmentation in the BD in AN and EDRec and only a trend was found in BN.

The results described above give evidence to suggest that weak central coherence fulfils the two first criteria for an endophenotype in ED: it is associated with the disorder in its active phase (in women with current AN and BN) and it is present when the illness is no longer active (after recovery).

A discussion of a few points that may add to a better understanding of how weak central coherence is present in people with ED follows below.

### 10.2.1 Relative differences among lifetime ED groups

Lifetime ED groups did not show major differences in performance on central coherence variables when compared to each other. Differences between groups are summarised as follows: the BN group showed the lowest accuracy in the EFT (more false claims) and the AN showed the lowest superiority in time required for the embedded figures in the EFT (statistical trend only). EDRec was the fastest among the ED groups. Few discrepancies in the central coherence profile were also found between sub-diagnostic categories (e.g. restricting versus purge-binge AN). However, the present study did not include sufficient numbers to disentangle these findings by sub-diagnosis (see Chapters 4 and 5).

### 10.2.2 Is weak central coherence ‘universal’ in ED?

One objective in this thesis was to explore whether weak central coherence was an underlying trait of ED. As ED are highly heterogeneous (Bulik *et al.*, 2007b, Lowe *et al.*, 2001, Steiger and Bruce, 2007) some individual differences were expected.

An individual examination of test results for both the ED and HC groups revealed that weak central coherence, although more common among those with lifetime ED, was neither universal nor specific to this group. Thus, some people with ED do not display the characteristic profile of weak central coherence and this profile is also present in a proportion of healthy individuals. On average, the proportion of women with ED that fulfilled the criteria for weak central coherence,



i.e. showed extreme ability in at least one local processing task AND weakness scores in at least one global processing task, was 58.7% whereas in the HC group only 16.7% met these criteria. Thus, the relationship between those having weak central coherence in the ED and HC populations is about 3:1. Similar results have been described in the ASD population for which the weak central coherence account has been proposed to explain most of their cognitive anomalies (e.g. Jarrold and Russell, 1997, Teunisse *et al.*, 2001).

An investigation within the ED group revealed that those with weak central coherence were younger, had a shorter duration of illness and had higher BMI. These results give some evidence in favour of the argument that weak central coherence is not a consequence of starvation associated with AN (see Chapter 4) and may not be a marker for chronicity as it has been argued (Madden, personal communication).

The analysis of the three components derived from the Principal Components Analysis (PCA, see Chapter 7) confirmed the heterogeneity in the profiles across groups. An analysis of factor scores was stricter than the one used for individual tasks as consistency across all tasks is required and also had the limitation of including all the ED samples in the factor extraction procedures instead of HC only. Having these issues in mind, individuals were categorised into four groups according to their scores in each factor (e.g. poor, low-medium, medium-high and high). Afterwards, combinations between good performance in local processing (over 50<sup>th</sup> percentile in each factor) and poor in global processing (below 50<sup>th</sup> percentile in global visual processing and verbal coherence) determined who might have weak central coherence. Under these stricter criteria only 29.4% in the ED and 16.7% in the HC were classified as showing weak central coherence. It is interesting to observe that the proportion of individuals with weak central coherence using both definitions was similar in the HC group whereas there was more of a discrepancy in the ED group. The heterogeneity of ED discussed in Chapter 1 may account for this finding in the cognitive profile. Also, it could be argued that task demands influence how individuals display the trait (see Chapter 7). The nature of the tasks, in terms of whether or not they force the individual to overcome their spontaneous bias, may greatly affect the performance.

In the field of ASD, where a broad battery of tests assessing weak central coherence was used, only 23% met criteria of weak central coherence (lower than reports on previous reports using fewer tasks which showed about 50% of the ASD

with weak central coherence) versus 6% in the HC group although differences with a typically developed group were found on most of the individual tasks. This again suggests that there is heterogeneous individual performance across tasks (Booth, 2006).

### 10.2.3 Potential confounders

The effects of age, intellectual ability, anxiety, depression and OCD symptoms were considered as potential confounders in the differences between ED groups and HC on central coherence performance. Also, the potential effect of use of medication, duration of the illness and age of onset on cognitive performance within the ED were analysed in this study. Few and overall weak associations were found. The most relevant findings on tasks that differentiated between groups were:

- Use of medication did not have an effect on cognitive performance
- BMI only was positively associated with the style index in the HC. No relationship between BMI and central coherence performance was found in the other normal weight groups (BN and EDRec).
- Overall OCI-R score was linked to higher SCT and two subscales of OCI were found to correlate with lower central coherence indices in the AN.
- Anxiety was linked to lower central coherence indices in BN.
- Duration of illness was positively associated with longer detection times in the EFT in AN and BN and higher local score in the SCT in the latter group.
- In the BN, those using multiple purging methods obtained lower central coherence indices in the RCFT.

A number of other relevant associations were found. Intellectual ability was associated in all groups with errors in the HRT. As groups were equivalent on this variable it was unlikely to have a differential effect on task results. However, it may explain the fact that HRT was one of the least sensitive tasks to differentiate between groups and ceiling effects were found in the four groups. The same may be argued for Un/seg BD, based on the block design sub-scale of the Wechsler Intelligence Scales which has been found to be one of the best predictors of general intellectual ability of this well known intelligence test (Lezak et al., 2004).

One potential confounder variable, which unfortunately was not measured in this project, is the ability to flexibly adapt the cognitive style according to task demands (e.g. set-shifting). This point becomes relevant in light of the results from individual task performance. It is interesting that the RCFT, although favoured by global processing, has been defined as an ‘open ended’ task (i.e. a task in which there is no implicit or explicit demand to use either local or global strategies for successful performance) (Happé and Frith, 2006), was the most reliable in terms of showing differences between HC and lifetime ED groups. However, in tasks in which there is an implicit requirement to use local or global strategies (e.g. EFT, BD and HRT) there was more variation between individuals and groups. Booth (2006) found that high-functioning ASD (those with a normal intellectual ability) seemed to have a better understanding of implicit task demands and might be able to change the cognitive strategy accordingly thereby overcoming the default cognitive biases. Similar circumstances are likely to have taken place in the high intellectual groups that participated in the present study. Therefore, it might be hypothesised that individual differences in the ability to switch between styles of processing to adapt to task demands (set-shifting) may have influenced task results in people with weak central coherence. For example, performance in the Un/seg BD seems to require both local and global processing and switching between both at different stages of solving the task. In one person with weak central coherence, whose default style is to focus in detail, a delayed set-shifting would make performance poorer in terms of time although the task would be solved in the end. Similarly, errors in the HRT may be the result of an interaction between the default local processing and delayed set-shifting ability. This may explain the higher proportions of self-corrections found in the ED groups. Finally, as mentioned in Chapters 4 and 5, poor performance on the SCT in ED people might also reflect the interaction with poor set-shifting as the number of local responses was rare and most of the variance in the difference between HC and ED groups was due to long hesitations in finding an appropriate, coherent answer. On the contrary, tasks such as the RCFT more consistently showed the local bias in the ED group as there is no implicit requirement for local or global processing on the task and the default style is displayed. In the case of EFT, the required style is local processing in which people with ED are advantaged and performed much faster than the HC.

#### 10.2.4 Weak central coherence and its relationship with other cognitive functions in ED

From the results of this thesis, links between the current evidence of cognitive processing anomalies in ED and the evidence of weak central coherence can be made.

Firstly, the AN group, although superior to the HC group in detail processing, did not show the outstanding speed demonstrated by the normal weight groups. It has been argued that reaction times and motor speed are critical in the performance of most neuropsychological tasks (Lauer, 2002). This observation suggests that perhaps malnutrition interferes with superior local processing by affecting motor speed, explaining why the acute AN group had the lowest degree of superiority. Also, slowness in motor speed has affected performance in the BD task in this study. However, neuropsychological studies have found conflicting findings regarding the impairment of AN in tasks involving motor speed. Finger tapping and dysdiadochokinesis tests are slowed (Gillberg *et al.*, 1994a, Green *et al.*, 1996, Kingston *et al.*, 1996, Szmukler *et al.*, 1992, Tchanturia *et al.*, 2004c). However, no impairments have been found on visual-motor tasks such as digit symbol and Trail Making Test - A (Murphy *et al.*, 2002, Witt *et al.*, 1985) and faster psychomotor function has been found in the drawing task (Pieters *et al.*, 2003). In the present study, motor speed was uncontrolled therefore this explanation remains as a hypothesis.

Secondly, it might be possible that weak central coherence accounts for part of the impairments in visual-spatial functioning found in ED. For example, deficits in global processing may account for deficits in tasks that benefit from global integration such as drawing tasks (Bowers, 1994, Gillberg *et al.*, 1996, Key *et al.*, 2006).

Mediation analyses performed in this thesis with the RCFT data, showed that weak central coherence accounted for part of the deficit in non-verbal memory in people with AN and BN (Murphy *et al.*, 2002, Pendleton Jones *et al.*, 1991). Other working memory deficits (e.g. Green *et al.*, 1996, Kingston *et al.*, 1996) may also be explained by weak central coherence as it is supposed that a fragmented

informational processing would overload working memory capacity making it less efficient.

Thirdly, poor vigilance found in acute AN and BN may also be associated with weak central coherence e.g. the inability to filter out irrelevant stimuli or enhanced distractibility (Dickson et al., 2008). The reduced ability to integrate information may make it difficult to sustain attention in BN and AN (Laessle *et al.*, 1990, Laessle *et al.*, 1989, Seed *et al.*, 2000, Seed *et al.*, 2002) although there is inconsistency in the reports related to this deficit (e.g. Bayless *et al.*, 2002, Pendleton Jones *et al.*, 1991, Seed *et al.*, 2002).

Fourthly, another finding in the literature that may relate to weak central coherence is the enhanced functioning in effortful tasks that required a narrow focus of attention and difficulties in incidental learning or non-effortful task that may require better global abilities (e.g. Galderisi *et al.*, 2003, Strupp *et al.*, 1986).

Finally, as discussed before (see section 10.2.3) it seems plausible that the individual differences in test performance of people with ED on the weak central coherence battery may be partly explained by interactions with the ability to set-shift. The default cognitive bias for details can be overcome with some effort when individuals are asked to do so (Happé and Frith, 2006). Thus, women with weak central coherence and good set-shifting would be able to respond quicker to tasks where global demands are imposed and those with poorer set-shifting would take longer. Therefore, it would be argued that some of the heterogeneous profile shown by people with ED in this study might respond to the interaction between set-shifting and weak central coherence rather than to weak central coherence per se. This hypothesis may be critical to explore in future research.

#### 10.2.5 Central coherence as a unitary or dimensional concept

Although the question of the unitarity of the concept of central coherence was not related directly with the aims of this thesis, it has been addressed within the limited possibilities of this thesis, in order to contribute to the broader and ongoing discussion about this concept. The relevance of this question relates to the original description made by Frith (Frith, 1989) who described the drive for meaning (central coherence) as a cognitive style that would work as an umbrella affecting the overall functioning of individuals. In Chapter 7 there was an attempt to address this question

via examining the common underlying factors of the tasks used in this study across visual and verbal domains. A Principal Component Analysis revealed three clearly different factors underlying the performance of all the central coherence tasks (i.e. verbal coherence, and visual local and global processing factors). This finding does not support the unity of the concept. The hypothesised trade-off relationship between local and global processing in women with ED was not supported either. Analyses showed that on the contrary, local and global processing, at least in the visual domain, tended to go together in the general sample of participants and in ED in particular. Thus, good local processing would not be reached necessarily at the expense of poor global processing but the two abilities, although independent, are positively associated. However, it is necessary to remind the reader that it was not possible to perform factor extraction properly and the ED sample was over-represented in the data included in the PCA. There was some support for central coherence across modalities (verbal and visual) but an apparent lack of power prevented the making of a stronger statement.

In sum, there is some indication that local and global processing are positively related. Also, there is some evidence for the drive for coherence across domains (verbal and visual). These results suggest that central coherence was a dimensional concept (versus unitary) formed by related but independent skills that separately contribute to the overall cognitive style of individuals. A bigger study with tasks that measure 'pure' local and 'pure' global processing in difference domain would be needed to clarify this conceptual debate.

In ASD studies, healthy control groups have also shown positive associations between local and global processing (Happé and Booth, 2008). In the ASD population, however, the scenario is less clear. Some have argued in favour of a unitary concept with a trade-off between local and global processing (Booth, 2006, Teunisse *et al.*, 2001). Nevertheless, an alternative hypothesis is that the characteristic cognitive processing consists of an enhanced local processing unlinked with poor global processing (Mottron *et al.*, 2003, Mottron *et al.*, 2006, Plaisted *et al.*, 1998). Finally, pervasive weak central coherence across domains has also been found in some but not all the studies (e.g. Booth, 2006, Pellicano *et al.*, 2005, Ropar and Mitchell, 2001).

#### 10.2.6 Directions for future work

The conclusions derived from the study of the first objective of this thesis may have several implications for future research. Some of them are addressed below.

The first objective of this thesis was to demonstrate whether weak central coherence fulfilled the two first criteria for an endophenotype. The results from this thesis show that weak central coherence is associated with the illness and it remains present even when the illness is not active. Therefore the two first criteria in support of the hypothesis that weak central coherence is an endophenotype have been met. Further exploration would involve testing the hypothesis that weak central coherence is present at a higher level in unaffected relatives than in the general population, whether it is heritable, and if it is linked with ED in family members (Gottesman and Gould, 2003).

This thesis also shed light on some issues that need to be considered for future research using the endophenotype approach. Those individuals suffering from the illness showing weak central coherence may represent a specific genetic sub-group. Questions remain such as which sub-group would be more likely to exhibit the trait? What are the common characteristics of this sub-group?

The selection of the tasks measuring this trait may need some revision (e.g. adding measures of ‘pure’ global processing such as the Fragmented Pictures (Snodgrass et al., 1987) and more appropriate verbal tasks). Finally, the inclusion of measures of set-shifting would help to clarify the interaction between weak central coherence and executive functions and how this is expressed in cognitive performance.

Cross-sectional studies are useful as a preliminary exploration. However, in order to address with certainty issues such as the state versus trait status of any characteristic, the use of longitudinal studies is required. Developmental studies would illuminate factors of risks associated with weak central coherence. For example, Favaro *et al.* (personal communication) have found pregnancy complications linked to weak central coherence supporting the neurodevelopmental hypothesis of ED and highlighting environmental interactions relevant for weak central coherence.

Neuroimaging may help to better understand the mechanisms associated with weak central coherence in ED as seen in the limited studies in ASD (see Chapter 1). Imaging studies have made substantial advances in understanding differences in brain processes associated with cognitive anomalies in people with current or past ED (Key *et al.*, 2006, Lask *et al.*, 2005, Uher *et al.*, 2003, Wagner *et al.*, 2007) when looking for cues of aetiological and maintenance aspects of ED. Thus, imaging studies might be helpful in studying brain activation patterns linked to performance in central coherence tasks, to see whether compensatory mechanisms are apparent in those with weak central coherence in comparison with those who do not have the trait and overall, to understand the neurobiological mechanism behind the trait.

Another remaining question is how weak central coherence puts people at risk. One hypothesis is that weak central coherence underpins obsessive-compulsive personality traits, such as perfectionism and rigidity, which are part of the maintaining factors described in the Maudsley Model. Unfortunately we were unable to test this hypothesis as this thesis did not include a specific exploration between those personality traits and cognitive performance. However, the fact that cognitive aspects related with Autistic-type traits (cognitive rigidity and attention to details) were inversely associated with global processing in both visual and verbal domains, gives some support to this hypothesis.

Finally, many other questions remain unanswered and would merit some exploration in future research. For example, does weak central coherence predict outcomes in ED (symptomatic and general e.g. quality of life)? Is weak central coherence even 'weaker' in males with ED and more similar to ASD patients? How does weak central coherence interact with other traits in ED (e.g. distortion in body image, rituals around food and weight, excessive exercise, denial of illness severity, etc.)? Would it be possible to prevent the development of an ED using targeted interventions in individuals that display weak central coherence and other risks for ED?

Future directions for research pertaining to how the weak central coherence account may be involved in treatment are discussed in the following section (see section 10.3.4).



### **10.3 Implications and Applications of the Weak Central Coherence Hypothesis in the Treatment for Eating Disorders: Two pilot Experiences**

To be able to address the second objective of this thesis, two pilot studies involving the development and implementation of modules of treatments that incorporated the concept of weak central coherence into clinical practice were conducted in collaboration with the supervisors of this thesis (Dr. Kate Tchanturia and Prof. Janet Treasure). A simple pre and post intervention design was employed in the study of Cognitive Remediation Therapy module (CRT) and a pre-post and follow-up design was used in the Motivational Enhancement Feedback module. Data were analysed with quantitative paradigms.

The pilot CRT study mainly looked into the effectiveness of the intervention in improving cognitive test performance and at evaluating possible relationships between improvements and clinical features (e.g. anxiety and depression). Also, a relationship between aspects of satisfaction with the intervention and improvements in cognitive test performance was addressed in order to explain mechanisms of change. This study was part of a bigger project in CRT for ED which also included set-shifting remediation.

The brief feedback intervention was in an earlier stage of development. Therefore, this pilot study was aimed at developing it further and examining its acceptability and effectiveness in terms of improvements in awareness of the role of extreme bias in information processing in real life.

Overall, both interventions centred on cognitive styles were highly valued and accepted by patients, thereby corroborating the results of previous research using CRT in small case studies (Davies and Tchanturia, 2005, Tchanturia *et al.*, 2007a, Tchanturia *et al.*, 2008, Tchanturia *et al.*, 2006b). Effectiveness was also found in terms of cognitive performance in CRT and improvements in some of the items of a self-report questionnaire administered in the feedback intervention. However, these studies remain at an early stage.

A summary of the characteristics of the proposed interventions and mechanisms of change are described below.

### 10.3.1 Objectives of these interventions

One of the main characteristics that differentiate these interventions from other previous treatments developed for ED is the focus on the *processes* of thinking rather than the *content*. This feature of the interventions presented here differs from traditional psychotherapies such as psychodynamic therapy and cognitive behavioural therapy (CBT) in which, to put it simply, emphasis is placed on content rather than underlying cognitive processes (Baldock and Tchanturia, 2007). Therefore, the development of interventions like CRT or feedback which address underlying processes of cognitive and behavioural aspects of the ED seem to complement the current treatment strategies and open up a new area of intervention which is evidence- and theory-based (Lopez *et al.*, 2008d). The focus on the process rather than the content of the psychopathology may help patients to step back and understand the mechanism whereby they are trapped within the illness. It was proposed that this type of interventions may be more acceptable at the beginning of the treatment especially when patients are in the pre-contemplation stage of the cycle of change (Prochaska and Diclemente, 1994).

### 10.3.2 Characteristics of the interventions

As mentioned above these interventions have both similarities and differences, which are summarised in Table 10.1. For more details see Chapters 8 and 9.

**Table 10.1 Differences and similarities between CRT and Feedback Intervention**

	<b>Cognitive Remediation Therapy</b>	<b>Brief Feedback Intervention</b>
Target population	Severe AN admitted to an specialist EDU	Any ED (including EDNOS) seen in outpatient settings
General objective	Target process rather than content of thoughts (the ‘how’ versus ‘what’ of thinking)	Same
Objective	Improve cognitive flexibility and global processing	Same
Mechanism of intervention	<ul style="list-style-type: none"> <li>▪ Interactive cognitive exercises</li> <li>▪ Reflection on cognitive styles</li> <li>▪ Individualised formulation</li> <li>▪ Behavioural experiments</li> <li>▪ Problem solving</li> <li>▪ Letters that summarise treatment process at the end of CRT</li> <li>▪ Metacognitive reflection</li> </ul>	<ul style="list-style-type: none"> <li>▪ Motivational Interviewing techniques</li> <li>▪ Feedback on neuropsychological assessment with norms</li> <li>▪ Individualised formulation</li> <li>▪ Reflection on role of cognitive bias in development and maintenance of the illness and general functioning</li> <li>▪ Behavioural experiments</li> <li>▪ Problem solving</li> <li>▪ Letter of formulation and end</li> </ul>
Inclusion of sensitive issues (ED symptoms and emotions)	These issues are explicitly left out of the intervention	These issues are included in the intervention as a core part of the reflection
Duration	Pre, post and follow up assessment session: 50 min each 10 weekly sessions; 45 min each Maximum length of intervention: 12 weeks	Pre, post and follow up assessment: 50 min first assessment, 20 mins post and follow up assessments 2 sessions: motivational feedback and reflection: 1 hour each Maximum length of intervention: 4 weeks
Who can deliver the intervention	Nurses, assistant psychologists, researchers, social workers, etc under close weekly supervision of an experienced clinician	Clinicians with training in motivational interviewing
Materials	Manual and copies of exercises	Feedback in the form of charts Brief manual for clinicians Worksheet for patients
Time in treatment	Soon after admission to the inpatient unit	Generally used before commencing standard treatment
Other	Involves neuropsychological assessments (pre-post-follow-up) Does not include feedback on neuropsychological performance	Involves neuropsychological assessment (pre intervention only) Does include feedback on neuropsychological performance

### 10.3.3 How to integrate these interventions into the general treatment?

It is still uncertain at what stage in the treatment interventions centred in cognitive styles may be most useful and whether this should be part of the standard treatment or only given to those that show indices of weak central coherence after a neuropsychological assessment. So far, these interventions have been tested in the initial stage of treatment. One possibility is to offer these interventions as pre-therapy modules that facilitate the effectiveness of further, more complex psychotherapeutic interventions (Pretorius and Tchanturia, 2007). Under extremely exceptional circumstances, however, a module of cognitive intervention, such as a brief feedback module, might be enough for some patients to start the recovery process with minimal further professional support (Lopez *et al.*, 2008a). CRT might not be suitable as a stand-alone therapy as it has been specially designed as an intensive module for severely impaired patients who in the main would need more complex interventions. However, shorter versions of CRT may also be of use in out-patient settings (Baldock and Tchanturia, 2007).

### 10.3.4 Clinical implications and future directions

There are some implications for research and future developments of the interventions for ED that emerge from these pilot studies. Some of them are mentioned below.

More work needs to be done in order to understand how improvements in the use of cognitive styles such as central coherence relate to changes in ED psychopathology and general functioning. Multidimensional assessment approaches that include behavioural, cognitive, affective and neurobiological examinations may increase this understanding. For example, little is known about neurobiological correlates of weak central coherence (Happé and Frith, 2006) and nothing about brain mechanisms related to improvements in the use of global strategies of thinking.

Neuroimaging in AN, has however, shown relationships between biological correlates of the illness and neuropsychological functions (Lask *et al.*, 2005, Wagner *et al.*, 2008, Wagner *et al.*, 2007) therefore it would be expected that treatments that affect neuropsychological functioning will impact on brain functioning. Also, further examination into mechanisms of change in both, but particularly in the feedback intervention, needs to be done.

Some of the questions that remain unanswered and might be of relevance for future advances in this type of targeted interventions are: do cognitive exercises produce changes in the use of global strategies or is it reflection on cognitive styles and the planning of different strategies that drive these changes? Also, does the involvement/exclusion of sensitive issues related with the eating symptomatology relate to better or poorer outcomes? A study that compares these two interventions with specific outcome measures may help to answer these questions.

The development of complementary clinical modules that target other relevant maintaining factors, as is proposed in the new Maudsley model of maintenance of ED (Schmidt and Treasure, 2006), may increase the possibility of finding more effective treatment strategies especially for AN, where effective treatments are urgently needed (Bulik *et al.*, 2007a, NICE, 2004). For instance, Dr. Tchanturia and collaborators are developing a new module that adds aspects of social and emotional processing to CRT as this is an area in which at least a sub-group with ED show tremendous difficulties such as increased alexithymia (Rastam *et al.*, 1997, Zonnevijlle-Bender *et al.*, 2002), high anxiety (Strober *et al.*, 2007, Zonnevijlle-Bender *et al.*, 2002), high social anxiety (Hinrichsen *et al.*, 2003) and difficulties in social cognition (Zucker *et al.*, 2007).

The Eating Disorders Unit at the Institute of Psychiatry has also developed a series of interventions to address carers' needs as it has been shown that close others' responses to the illness may act as another maintaining factor (Sepulveda *et al.*, 2008, Treasure *et al.*, 2007b).

How these interventions may be incorporated into an effective treatment is still uncertain. One possibility is that a broader individual assessment will provide clinically relevant information to prioritise areas of intervention according to each patient's needs. A continuing evaluation of the processes of change may guide better clinical decisions. The development of modules of treatment such as those presented here might allow more flexibility in the delivery of more appropriate treatment for each patient, as well as have reduced individual and social costs in the long-term. Such a model, however, requires the availability of thoroughly trained and supervised research/clinical assistants to carry out these time consuming assessments. Therefore, the development of new technologies for assessment, such as online/computerised standard assessments that reduce the need for specialised assessors may help. Modules of self-help interventions based on multimedia would

also increase the possibilities of offering better access to and uptake of treatment (Schmidt and Varinia Sanchez-Ortiz, 2007).

Finally, interventions that focus on cognitive styles have been used in obsessive-compulsive disorders with success. Park and collaborators developed a cognitive training programme for people with OCD. The training group had a decrease in clinical symptoms and also improved their recall accuracy in the RCFT (Park et al., 2006). Also Buhlmann *et al.* (2006) developed a brief module targeting organisational strategies with positive results in terms of improving test performance. These findings suggest that interventions with a focus on basic information processing anomalies may have a promising potential for improvement in ED and OCD spectrum disorders and endorse the hypothesis of a common endophenotype between these disorders.

## 10.4 General Limitations of this Study

Limitations of the specific studies described in chapter 4, 5, 6, 8 and 9 were discussed as appropriate in each research chapter. Therefore, only a broader discussion of main limitations is provided below.

### 10.4.1 Recruitment bias

As described in the Methodology Chapter (see Chapter 3), a great effort was made in this study to reduce sampling bias in terms of the most chronic ED cases who attend the clinics associated to the Institute of Psychiatry. To overcome this potential bias, the volunteer database held in the EDU was utilised as well as advertisements on the IoP web site for general community samples. Despite this effort, the groups of women participating in the study tended to have a chronic and severe (e.g. high co-morbidity) illness. This may relate with self-selection bias usually found in studies in psychiatric populations. It might be possible that those with longer history of the illness are more motivated to help in research from their own experience with the illness. Usually, participants emphasised that their motivation to take part in the study stemmed from their experience of struggling to get well. They also acknowledged that the theme of this project, cognitive aspects of the illness, was novel and found it promising in contributing to the understanding of the illness.

To overcome the bias imposed by self-selection a true community sample e.g. cohort of patients would help (e.g. Gillberg *et al.*, 1994b).

### 10.4.2 Confounding variables

Neuropsychological performance involves a number of potentially confounding variables needed to be taken into account such as intellectual ability, co-morbid conditions, age, chronicity of the illness, etc. In this study, history of head injury and neurological illness, and psychosis were excluded. The main co-morbid conditions associated with ED were examined as to their potential confounding role as were demographic and other clinical variables such as BMI and use of medicines. Unfortunately, the skewed distribution of data precluded the use of more

sophisticated statistical analysis for most of these variables (e.g. analysis of covariance). Thus most of the relationships between cognitive performance and potential confounding variables were examined through simple binary correlations. Whenever possible, groups were divided according to the relevant variable (e.g. use of medicines) and comparisons between groups were carried out.

Previously, we have discussed the potential implications of set-shifting abilities in performance on central coherence tests. Other unexplored possible confounding variables such as pregnancy and perinatal complications were not included. For example, maternal stress in the second trimester of pregnancy has been associated with weak central coherence in patients with AN. A more extensive and careful screening that considers valid retrospective information would contribute greatly to the understanding of variables linked to weak central coherence in the ED population.

#### 10.4.3 Recovery

Despite the attempt to identify fully-recovered ED cases based on established criteria (Kaye *et al.*, 2008, Kordy *et al.*, 2002, Wagner *et al.*, 2006a), cross-sectional designs as used here are not the most sound methodology to explore state versus trait effects. Longitudinal studies are proposed as the gold standard for such explorations but difficult to implement in disorders such as ED where a chronic course of the illness is common and recovery takes place over an extended time frame. This limitation was addressed in detail in Chapter 6.

#### 10.4.4 Sample size

From the results of this thesis it was apparent that some of the measured variables did not reach statistically significant differences between ED and HC groups and between sub-categories within the ED group. In a few of them this lack of power was anticipated as initial power calculations based on a pilot study demonstrated the need for numbers that were completely beyond of the possibilities for this thesis. This was the case of the Block Design task which consistently did not reach statistical significance with most of the ED samples.

More importantly, ED groups were mixed in terms of sub-categories, e.g. PAN, RAN, or PBN or RBN, EDRec with AN or BN past history. Analyses trying to separate the effect of sub-diagnosis found trends in a few variables. Therefore, larger



sample sizes would enhance the power to detect subtle differences within ED categories.

#### 10.4.5 Central coherence battery

Several issues related with the suitability of the tasks used in this study have been discussed through the thesis. The main difficulties can be summarised as the lack of ‘pure’ tasks. However, it is known that most neuropsychological tasks involve more than one cognitive function at a time (Strauss et al., 2006). Also people often solve tasks and reach similar goals via different mechanisms (Happé and Frith, 2006). Most of the tasks utilised here have been modified in order to isolate as much as possible, indices of central coherence from other possible confounders (see Chapter 3). The tasks that detected more reliable differences between groups were the RCFT (with specific indices to target central coherence independently of other aspects measured by the tasks) and the EFT (which was modified to address superior detection of details only).

A caveat in this thesis was the use of verbal coherence tasks that were promising in the study of people with ASD but seemed to be easy to solve for people with normal intellectual abilities. Thus, both the SCT and the HRT showed ceiling/floor effects in the studies with ED samples. The California Verbal Learning Test (Delis *et al.*, 1987) that have been used in an OCD population (Savage et al., 2001), may be a more appropriate task to measure central coherence in a population with normal intellectual ability.

#### 10.4.6 Design of pilot studies to test clinical interventions

Limitations on the design of the two pilot studies presented in the thesis were discussed in the appropriate chapters (Chapters 8 and 9). Improvements of the methodological flaws of the present studies may include the use of larger sample sizes, randomised controlled trials, and advances in the assessment measures that allow for a better understanding of how interventions targeting cognitive processing relate to clinical recovery.

## **10.5 Concluding comment**

This thesis represents a unique contribution in the field of ED and has shown how cognitive traits may be associated with the development and maintenance of ED. Specifically, this thesis systematically has explored the concept of weak central coherence and has pioneered the endophenotype approach for central coherence in ED.

The topic of weak central coherence arose from studies that suggest a link between AN and ASD in terms of a clinical and cognitive test performance profile. The weak central coherence hypothesis also fitted well with many clinical observations of behavioural and cognitive features of people with ED.

The results of this thesis provided evidence to suggest that at least a subgroup of women suffering from an ED have weak central coherence. This cognitive bias was also found in women after recovery. Altogether, these findings gave support that warrants the continuation of the endophenotype examination of weak central coherence in ED.

The thesis also advances the field in demonstrating how neuropsychological studies in ED may successfully inform treatment strategies. Cognitive assessments and targeted interventions based on principles of cognitive remediation can be incorporated into standard care. Interventions that address underlying mechanisms rather than evident features of the illness seem to give a unique opportunity to patients to examine the way they function and how this relates with the illness and their general life in a non-threatening manner.

It is hoped that this thesis has contributed to a better comprehension of the complex cognitive aspects associated with ED and emphasised the importance of incorporating the role of cognitive functioning in the understanding of the psychopathology of the illness, its development and maintenance, and the relevance of addressing them in the treatment.

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## **APPENDICES**

**Appendix A Modified Eating Disorders Examination Questionnaire  
(EDE-Q4)**

Eating Disorders Examination Questionnaire (EDE-Q 4)

Study No. 020/05

Age .....Date of birth ...../...../.....

Gender: M / F

Current height.....Feet/inchesor.....Metres

Current Weight: .....Stones/pounds or .....Kg

What is the heaviest you have weighed at this height?.....Stones/pounds or  
.....Kg

What is the lightest you have weighed at this height? .....Stones/pounds or  
.....Kg

Current medication (please list *all* medications, including herbal remedies or  
supplements)

.....  
.....  
.....

Please circle appropriate answer:

Have you started your menstrual periods? Yes / No

If yes how many menstrual periods have you had in the last 3 months? 0 /1/ 2 / 3

Are you currently using the oral contraceptive pill? Yes / No

Are you currently using any other hormonal contraceptive such as depot provera?  
Yes / No

Have you ever missed at least 3 consecutive periods while not pregnant? Yes / No

Have you been through the menopause? Yes / No

## Past Eating Questionnaire

### Instructions

The following questions are concerned with your eating habits in the past.

Please answer all the questions.

**Has there ever been a time in your life when you have deliberately tried to limit the amount of food you eat everyday for at least three months?**

(Please put appropriate number in box)

0 – no

1 – yes[ ]

**Have you ever not eaten for more than 8 hours at least twice a week, for three months or more?**

0 – no

1 – yes[ ]

**In the past, have there been any times when you have felt that you have eaten what other people would regard as an unusually large amount of food given the circumstances? (Please put appropriate number in box)**

0 – no

1 – yes[ ]

**If yes what was the maximum number of times this happened in any three-month period?**

/ 3 months

**During how many of these episodes of overeating did you have a sense of having lost control over your eating?**

**In the past, have you had other episodes of eating in which you have had a sense of having lost control and eaten too much, but have not eaten an unusually large amount of food given the circumstances?**

0 – no

1 – yes[ ]

**If yes what was the maximum number of times this happened in any three-month period?**

/ 3 months

**In the past have you made yourself sick (vomit) as a means of controlling your shape or weight?**

0 – no

1 – yes[ ]

**If yes what was the maximum number of times this happened in any three-month period?**

/ 3 months

**In the past have you taken laxatives as a means of controlling your shape or weight?**

0 – no

1 – yes[ ]

**If yes what was the maximum number of times you took laxatives in any three-month period?**

/ 3 months

**In the past, have you taken diuretics (water tablets) as a means of controlling your shape or weight?**

0 – no

1 – yes[ ]

**If yes what was the maximum number of times you took diuretics in any three-month period?**

/ 3 months

**In the past have you exercised hard as a means of controlling your shape or weight?**

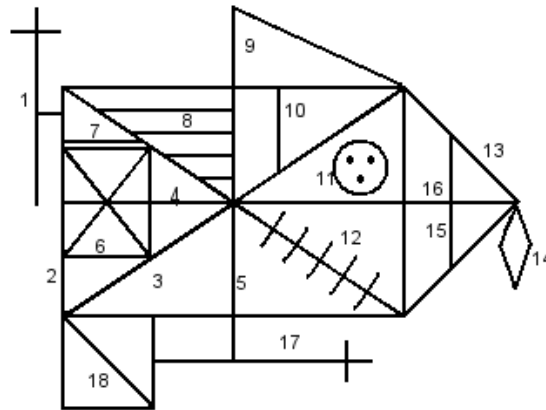
0 – no

1 – yes[ ]

**If yes what was the maximum number of times you exercised in any three-month period?**

/ 3 months

## Appendix B Scoring details for Rey-Osterrieth Complex Figure Test for Accuracy



Each element of the figure above is awarded with 0 to 2 points according the accuracy of drawing as follows:

1	Accurately drawn - Incorrectly placed
1	Inaccurately drawn - Correctly placed
0.5	Inaccurately drawn, but recognisable - Incorrectly placed
0	Inaccurately drawn, and unrecognisable, or omitted - Incorrectly placed

The following table shows a description of each element that guides the accuracy scoring (Lezak *et al.*, 2004, Spreen and Strauss, 1998, Strauss *et al.*, 2006).

	<b>Element</b>	<b>Description</b>
1	<b>Vertical Cross</b>	The cross must come down to horizontal midline, and extend above the large rectangle; the line that joins cross to rectangle must be approximately in the middle of the cross, and must come between detail 7 and the top of the large rectangle
2	<b>Large Rectangle</b>	The horizontal dimensions must not be greater than twice the vertical dimensions of the rectangle; score 1 if rectangle is not complete in any way (or is a definite square shape)
3	<b>Diagonal Cross</b>	The diagonal cross must touch each of the four corners of the rectangle and intersect in the middle of the large rectangle
4	<b>Horizontal Midline of Large Rectangle</b>	The line must clearly go from midpoint of the left side of the large rectangle to the midpoint of the right side of the large rectangle in one straight line
5	<b>Vertical Midline of Large Rectangle</b>	The line must start at the midpoint of the bottom of the rectangle and go through in one straight line to the midpoint at the top of the rectangle
6	<b>Small Rectangle</b>	The top of the small rectangle must come between lines 2 and 3 of detail 8; the width should be approximately a quarter of the width of the large rectangle; the inside cross must come from the four corners of the rectangle, and intersect at the midpoint of the rectangle (on detail 4)
7	<b>Small Horizontal Line above Small Rectangle</b>	The line must be shorter than the horizontal aspect of detail 6, and should fall between the top of detail 6 and the 2 <sup>nd</sup> line of detail 8
8	<b>Four Parallel Lines</b>	Each line should be parallel with the spaces between them approximately equal
9	<b>Small Triangle above Large Rectangle</b>	The slope of the triangle should not be the same as the slope of triangle 13; the height of the triangle should not be greater than its base.
10	<b>Small Vertical Line within Large Rectangle</b>	The line should be clearly shifted to the left
11	<b>Circle with Three Dots</b>	The circle must not touch any of the sides; two dots above and one dot below.
12	<b>Five Parallel Lines</b>	The lines must not touch any sides and should be in approximately equal distance from each other
13	<b>Sides of Large Triangle attached to Large Rectangle</b>	The height of the triangle must not be greater than half of the horizontal midline of the rectangle
14	<b>Diamond</b>	The element should be diamond in shape; attached to the end of 13 and not extend below the bottom of the large rectangle



<b>15</b>	<b>Vertical Line within Sides of Large Triangle</b>	The line must be parallel to side of large rectangle; must be shifted to the left within detail 13; must be in one line
<b>16</b>	<b>Horizontal Line within Sides of Large Triangle</b>	The line must come from the midpoint of the right side of the large triangle and extend to the top of triangle 13
<b>17</b>	<b>Horizontal Cross</b>	The right side of the cross must be clearly longer than the left side of the cross, but not extend beyond the large rectangle; should start at the midpoint of the right side of the square (element 18)
<b>18</b>	<b>Square attached to Large Rectangle</b>	Must clearly be a square; sides should be the same width as detail 6; therefore a quarter of main rectangle

## Appendix C Sentence Completion Task: Local and Global Conflict Task

### Instructions

“You will hear some sentences and I ‘d like you to tell me something to finish off each sentence. First we’ll do one for practice:

“He cleaned up the mess with a brush and...”

Completions may be single words or a phrase. Try to prevent subject from repeating entire sentence. Scoring is based on the subject’s first response.

Sentence	Answer	Time	Score	Local
The woman went to the cinema and...				
On bonfire night children set off bangers and ...				
In a cave lived a bat and ...				
The burglar tried to open the safe and...				
We wake up when its day and...				
In the museum there are sculptures and...				
The teacher picked up the chalk and...				
In the morning the sun went up and...				
The old shoe-maker mended the shoes and...				
The United striker went for the ball and ...				
In the field by the lake was a horse and...				
The book was left on the table and ...				
In the sea there are fish and...				
The woman took the cup and...				
The fireman carried the bucket and...				
He broke the window with a hammer and...				
The sea tastes of salt and...				
In the zoo there are lions and...				
You can get burnt by the sun and...				
At the end of the day I like to read and...				
She tied up her hair with a bow and...				
I was given a pen and...				
The lion ran to join his pride and ...				
You can go hunting with a knife and...				
Little boys grow up to be men and...				
Total Score				
Total number local completions				

## Scoring

0	Correct global completion
1	Repetition or local associate to another word in sentence, no response, or long pause (more than 10 seconds)
2	Local completion to end of sentence

## Appendix D The Homograph Reading Test

### Instructions

“I am going to show you a list of words, what I want you to do is read each word out loud”

Word	Circle pronunciation	
	Frequent	Rare
Bow	Bo	b(owl)
Lead	Leed	led
Tear	Tear	tair
Row	Ro	r(owl)

“I am going to give you some sentences now, and I want you to read them out loud”

Present sentences one at a time in a set order. Tape record responses.

IP	SC		
		He took a <b>bow</b> from his music case	BF
		Mary wanted to take Rover for a walk, so she went to the cupboard and took the <b>lead</b>	AF
		The brothers started shouting. Tom left because he didn't want to be involved in a <b>row</b>	AR
		There was a big <b>tear</b> in her dress	BR
		It was the <b>lead</b> in the box that made it so heavy	BR
		Everyone who wanted to see the new film had to stand in a <b>row</b>	AF
		Jack went to speak to the King. Before he began his speech he made a <b>bow</b>	AR
		There was a big <b>tear</b> on her cheek	BF
		The scrap metal man first took the copper and iron and then he took the <b>lead</b>	AR
		The man had a second <b>row</b> with his wife the day after	BR
		He took a <b>bow</b> when everyone clapped	BR
		The girls climbed over the hedge. Mary's dress was spotless, but in Lucy's dress there was a big <b>tear</b>	AR
		It was the <b>lead</b> guitarist that sang at the concert	BF
		The cowboy with the gun won the fight because the Indian just had a <b>bow</b>	AF
		Molly was very happy, but on Lilly's cheek there was a big <b>tear</b>	AF
		The man had a second <b>row</b> seat in the cinema	BF

IP	Initial pronunciation correct: Yes✓ No x
SC	Self- Corrected : Yes✓ No x
↑	Mark point of correction on the sentence (start of repetition)
/	Hesitation or pause

## Appendix E Cognitive Styles in Action

Read each of the statements and mark the box that best describes your beliefs about your cognitive style at present.

	Statement	Strongly agree	Agree	Slightly agree	Slightly disagree	Disagree	Strongly disagree
	My strength lies in an eye for detail –I don't easily see the big picture						
	My strength lies in being able to grasp links & connections-I have to make a special effort to focus on detail						
	I often notice things that other people have missed						
	I am good at keeping my eye on "the big picture"						

Read each of the statements and mark the box that best describes your beliefs and feelings about your behaviour and cognitive style at present.

	Statement	Strongly agree	Agree	Slightly Agree	Slightly disagree	Disagree	Strongly disagree
1P	Planning and organising day to day events is essential						
2C	I am confident that I can get by most things by the seat of my pants						
3I	It is important to be able to get to the essence of an idea and skip details						
4C	I feel confident that I can get to the essence even if I do not pick up on all the details'						
5C	I am able to reflect on my way of engaging with tasks so that it is fit for purpose						
6P	I expect the highest standard in everything I do						
7I	I consider it is important to be able to change the way I tackle a problem according to environment demands						
8C	I feel confident that I am able to change the way I tackle a problem according to what the environment demands						

Cognitive Styles in Action (continuation)

	<b>Statement</b>	<b>Strongly agree</b>	<b>Agree</b>	<b>Slightly Agree</b>	<b>Slightly disagree</b>	<b>Disagree</b>	<b>Strongly disagree</b>
9I	It is important to be able to zoom in for detail and out to see the bigger picture						
10C	I feel confident that I can zoom in for detail and out to see the bigger picture when required						
11P	When I am working on something, I cannot relax until it is perfect						
12P	People around me think I am still competent even if I make a mistake						
13I	It is important to be flexible and to be able to change from one activity to another						
14C	I am able to change quickly from one activity to another						
15I	I think it is important to be able to switch from getting things carefully planned to doing things on an impulse						
16C	I am confident that I can switch from getting things carefully planned to doing things on an impulse						
17I	When judging how much effort to put into a task I think it is important to see what is good enough rather than going for excellence						
18C	When judging how much effort to put into a task I am confident that I can decide to do what is good enough rather than going for excellence						
19P	I never aim for perfection in my work						
20P	It makes me uneasy to see an error in my work						
21P	I do not have to be the best at whatever I am doing						
	<b>TOTAL</b>						

Scoring:

Statements marked with *P* compose the *Perfectionism scale* (maximum score = 42);

Statements marked with *I* compose the *Importance scale* (maximum scores = 36);

and Statements marked with *C* compose the *Confidence scale* (maximum score = 48).