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Exploring the neurocognitive signature of poor set-shifting in anorexia and bulimia nervosa

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ABSTRACT

Poor set-shifting has been implicated as a risk marker, maintenance factor and candidate endophenotype of eating disorders (ED). This study aimed to add clarity to the cognitive profile of set-shifting by examining the trait across ED subtypes, assessing whether it is a state or trait marker, and whether it runs in families. A battery of neuropsychological tasks was administered to 270 women with current anorexia (AN) and bulimia nervosa (BN), women recovered from AN, unaffected sisters of AN and BN probands, and healthy control women. Set-shifting was examined using both individual task scores and a composite variable (poor/intact/superior shifting) calculated from four neuropsychological tasks. Poor set-shifting was found at a higher rate in those with an ED particularly binge/purging subtypes. Some evidence for poor set-shifting was also present in those recovered from AN and in unaffected sisters of AN and BN. Clinically, poor set-shifting was associated with a longer duration of illness and more severe ED rituals but not body mass index. In sum, poor set-shifting is a transdiagnostic feature related to aspects of the illness but not to malnutrition. In part it is a familial trait, and is likely involved in the maintenance of the illness.

1. Introduction

Psychiatric illnesses are complex both in terms of aetiology and presentation, making research based on overt clinical symptoms particularly challenging. An alternative strategy is to focus on underlying mechanisms such as maintaining factors and biological markers. The search for such markers is particularly applicable to the eating disorders (ED) given their unstable diagnostic categories (Anderluh et al., 2009) and the current lack of targeted and effective treatment (Bulik et al., 2007; Shapiro et al., 2007; Steinhausen, 2009; Treasure et al., 2009). One medium used to explore such mechanisms is that of neuropsychology (Gottesman and Gould, 2003; Ritsner and Gottesman, 2009), where standardised and systematic assessment allows for detailed exploration of altered cognitive functioning.

Cognitive flexibility or set-shifting is an aspect of executive functioning that has been implicated as a risk marker (Tchanturia et al., 2002), maintenance factor (Steinglass et al., 2006), biomarker (Lopez et al., 2008a) and candidate endophenotype of ED (Holliday et al., 2005). Difficulties shifting set have been found in women with current and past ED across a number neuropsychological tasks (Roberts et al., 2007; Tchanturia et al., 2005). Poor set-shifting has been found in unaffected sisters of women with anorexia nervosa (AN) (Holliday et al., 2005), providing some evidence for this cognitive feature as an endophenotype. Recent theoretical models of AN have highlighted the role of set-shifting in the illness, one implicating rigidity (poor set-shifting) as a maintenance factor (Schmidt and Treasure, 2006) and another suggesting that the presence of poor set-shifting provides evidence for disturbed neural pathways in the brain (Steinglass et al., 2006). Recent work in neuroimaging demonstrated the neural correlates of poor set-shifting in AN, with less activation of the ventral anterior cingulated striato thalamic network and greater activation of the fronto parietal circuits (Zastrow et al., 2009). One interpretation is that people with ED recruit more top down, effortful control in this type of task.

The aim of this study was to further explore and understand the cognitive profile of poor set-shifting using a battery of neuropsychological tasks investigating this concept in women with a current or past ED, their unaffected sisters, and a healthy comparison group. The specific primary aims were to explore set-shifting 1) across ED subtypes, 2) in the recovered state, and 3) within the family of the affected individuals. A secondary aim was to examine the relationship between set-shifting ability and clinical features.

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2. Method

2.1. Participants

Participants were 270 women with and without a lifetime ED diagnosis. Of the 98 women with a current ED, 35 had restricting type AN (ANR), 33 had binge/purging type AN (ANBP), and 30 had bulimia nervosa (BN; 13 or 43.3% with history of AN). A further 30 women were fully recovered from AN (ANrc; 18 ANR; 12 ANBP) defined as 1 year healthy body mass index (BMI; >17.5), regular periods, and no AN or BN behaviours (e.g. restricting, purging, excessive exercise). Fifty of those with a lifetime ED (30 AN, 20 BN) had a sister with no history of an ED who also took part. A healthy control (HC) comparison group ($n = 88$) consisted of women of similar age and educational background with no personal or familial history of psychological illness or head injury. All participants were female and of white European ethnicity.

Clinical participants were recruited through the South London & Maudsley NHS Trust ED Service, through a research volunteer register held within the service, and through advertisements on websites (www.b-eat.co.uk; www.eatingresearch.com). HC participants were recruited through various means such as an email circular sent to King's College London staff and students, the Institute of Psychiatry's community volunteer database (MindSearch), and flyers posted in public places.

HC were screened first for personal or family history of diagnosed mental illness, traumatic head injury, healthy BMI (17.5–25) and age (16–60) Secondly, HC were screened based on self-report measures of disordered eating (Eating Attitudes Test-26; EAT-26), obsessive–compulsive behaviour (Obsessive–Compulsive Inventory-Revised; OCI-R), and anxiety and depression (Hospital Anxiety and Depression Scale; HADS). HC scoring above the cut-off on one or more of these measures were excluded.

2.2. Measures

2.2.1. Neuropsychological assessment

The Trail Making Test (Reitan, 1955): The TMT is a traditional measure of shifting set, where first an 18-item alphabetical sequence (Trail A; A-B-C etc) then an 18-item alphanumeric sequence (Trail B; 1-A-2-B-3-C etc) are connected in order. A computerised version was employed here (Kravariti et al., 2003). The set-shifting outcome used here is a balanced variable of Trail B minus Trail A, to control for baseline motor speed.

Wisconsin Card Sorting Test (Heaton et al., 1993): The WCST entails matching stimulus cards with one of four category cards. The sorting rule (colour, shape or number) changes after 10 correct sorts. The set-shifting outcomes employed are the number of raw perseverative errors and the number of categories completed.

Brixton Task (Burgess and Shallice, 1997): This task requires the participant to predict the movement of a blue circle across 10 circles (numbered 1–10) presented in a 5 × 2 grid. The task instructions detail that the pattern will change throughout the task. The number of incorrect predictions (excluding the first change in each of the 9 sequences) is the measure of set-shifting.

Haptic Illusion (Tchanturia et al., 2004a): Participants are asked to judge the relative size of wooden balls rolled into each hand whilst their eyes are closed. After a habituation phase of two different sized balls (15 trials), two same sized balls are presented where set-shifting outcome is the number of perceptual illusions experienced (same sized balls perceived as different sizes).

2.2.2. Clinical features

The Structured Clinical Interview for DSM-IV Disorders (SCID) (First et al., 1997) module H as modified for the NIMH Genetics of Anorexia Nervosa study (Kaye et al., 2008) was administered to all clinical cases and unaffected sisters to determine current and lifetime ED pathology. Comorbid mood, anxiety and substance disorders were also assessed with the SCID. The Yale-Brown Obsessive–Compulsive Scale (Y-BOCS) (Goodman et al., 1989) and the Yale-Brown-Cornell Eating-Disorder Scale (YBC-EDS) (Mazure et al., 1994) were also administered to all clinical cases and unaffected sisters to measure the frequency, distress and impact of OCD and ED related preoccupations and rituals.

The HADS (Zigmond and Snaith, 1983), the OCI-R (Foa et al., 2002), the Childhood Retrospective Perfectionism Questionnaire (CHiRP) (Southgate et al., 2008) and the Rosenberg Self-esteem (Rosenberg, 1965) self-report measures were administered to all participants.

2.3. Procedure

Participants were posted information, consent and self-report questionnaires prior to the appointment. Weight and height for all participants was checked on the day of testing. Set-shifting tasks were administered in the following order: TMT, WCST, Brixton Test, Haptic Illusion task.

2.4. Statistical methods

Power analysis using nQuery software indicated that a sample size of 30 per group would have 80% power to detect group differences across neuropsychological tasks with a 0.05 significance level (two-tailed). Normality of the data was assessed between diagnostic groups for each of the neuropsychological tasks, as grouped analyses were planned (Tabachnick and Fidell, 2000) At least one group across each task was not normally distributed, therefore nonparametric tests (Kruskal–Wallis for group comparisons and Mann–Whitney *U* for post-hoc comparisons) were employed.

For a secondary analysis, a composite variable was created to split the sample into those with intact, poor or superior set-shifting across tasks using the distribution of the current HC group. This consisted of two steps. First, for each of the four neuropsychological tasks, the main outcome was re-coded as low if the score fell below 1 SD of the HC mean, moderate if it fell within one standard deviation either side of the HC mean, or high if it was greater than 1 SD above the HC mean (all variables were normally distributed in the HC group, and task scores varied in the same direction i.e. more errors = higher score). The moderate range (inclusive) for each task was as follows: TMT B-A 2.3–16.5; WCST perseverative errors 5–12; Brixton errors 6–14; Haptic perseverations 6–24.

Second, a composite score was created using these re-coded variables. Cases with two or more high scores across the four neuropsychological tasks were categorised as having 'poor set-shifting', and those with two or more low scores categorised as having 'superior set-shifting'. All other cases were considered to have 'intact set-shifting' i.e. scores were not consistently poor or superior. Pearson's Chi-square tests were employed to investigate differences in the number of cases with poor set-shifting across groups. Independent-samples *t*-tests were used to investigate clinical features by set-shifting ability (poor vs. intact).

Cohen's *d* effect sizes were calculated for each comparison with an effect size calculator, using either Chi-square output or descriptive statistics. Differences are defined as negligible (≥−0.15 and <0.15), small (≥0.15 and <0.40), moderate (≥0.40 and <0.75), large (≥0.75 and <1.10), very large (≥1.10 and <1.45) and huge (≥1.45). All analyses were carried out using SPSS version 16.0.