Clinical investigation of set-shifting subtypes in anorexia nervosa

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A B S T R A C T

While evidence continues to accumulate on the relevance of cognitive inflexibility in anorexia nervosa (AN), its clinical correlates remain unclear. We aimed at examining the relationship between set-shifting and clinical variables (i.e., eating psychopathology, depression, and personality) in AN. Ninety-four individuals affected by AN and 59 healthy controls (HC) were recruited. All participants were assessed using: Eating Disorders Inventory-2 (EDI-2), Temperament and Character Inventory (TCI), Beck Depression Inventory (BDI), and Wisconsin Card Sorting Test (WCST). The AN group scored worse than HCs on set-shifting. According to their neuropsychological performances, AN patients were split into two groups corresponding to poor ($N=30$) and intact ($N=64$) set-shifting subtypes. Interoceptive awareness, impulse regulation, and maturity fears on the EDI-2 and depression on the BDI differed across all groups (HC, intact, and poor set-shifting subtype). Self-directedness on the TCI differed significantly among all groups. Cooperativeness and reward dependence differed instead only between HC and AN poor set-shifting subtype. After controlling for depression, only interoceptive awareness remained significant with reward dependence showing a trend towards statistical significance. These findings suggest that multiple clinical variables may be correlated with set-shifting performances in AN. The factors contributing to impaired cognitive inflexibility could be more complex than heretofore generally considered.

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1. Introduction

Anorexia nervosa (AN), is a severe psychiatric illness characterized by restricted eating, relentless pursuit of thinness, and obsessive fears of becoming fat in spite of life-threatening underweight (Yager et al., 2012). Several lines of evidence suggest that some clinical aspects of AN could mirror alterations of cognitive functions; in particular, those rigid and perfectionistic features that usually characterize affected individuals could be the result of set-shifting inefficiencies (Roberts et al., 2007).

In more detail, cognitive flexibility or set-shifting refers to the process of "shifting" and moving back and forth between different cognitive strategies and behaviors in response to changes in the environment. This cognitive ability has been found to be altered with a high degree of consistency in adults with AN (Tchanturia et al., 2011, 2012; Galimberti et al., 2013; for a review see Jáuregui-Lobera (2013). Interestingly, our group (Abbate-Daga et al., 2011) demonstrated that adult AN patients are rigid not only in verbal but also in non-verbal domains, as recently confirmed (Pignatti and Bernasconi, 2013). Still, cognitive alterations have been found

to play a role not only as vulnerability and maintaining factors but also as biological markers (Steinglass et al., 2006; Galimberti et al., 2012; Roberts et al., 2013).

Notwithstanding the body of evidence supporting cognitive inflexibility in AN, several aspects are still far from being conclusive. First, altered set-shifting is very common in adults diagnosed with AN although it does not characterize all affected individuals (Rose et al., 2012). Second, the role of depression on neuropsychological performances remains unclear although a clarification of this issue would be much needed (Giel et al., 2012) also given its frequent comorbidity with AN (O'Brien and Vincent, 2003). In fact, some studies failed to find an effect of depressive comorbidity on neuropsychological aspects (Sarrar et al., 2011; Calderoni et al., 2013; Sato et al., 2013) but the majority of the studies did not take comorbidity into account.

In addition to comorbidity, evidence accumulated on the key-role of personality in EDs (Amianto et al., 2011; Lilenfeld, 2011; Keel and Forney, 2013). Studies using the Temperament and Character Inventory (TCI; Cloninger et al., 1993) demonstrated that individuals with Eating Disorders (EDs) tend to be inhibited (high harm avoidance), perseverative (high persistence) and with low self-directedness (Fassino et al., 2004; Lilenfeld, 2011). Additionally, a "maladaptive" profile (Krug et al., 2011) characterizes a subgroup of patients with low reward dependence. However, to

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date the influence of personality on neuropsychological perfor-mances has received only scant attention.

Perfectionism represents a vulnerability and maintaining factor for different mental disorders including EDs (Egan et al., 2011) but its relationship with set-shifting is still far from being conclusive, particularly as regards AN (Pignatti and Bernasconi, 2013). To date, perfectionistic traits have been found not only to be positively related to cognitive rigidity (Ferrari and Mautz, 1997; Bühren et al., 2012) but also to play a role in action monitoring in depressed samples (Schrijvers et al., 2010). Individuals affected by Obsessive–Compulsive Disorder (OCD) tend to be characterized by both perfectionism and sub-optimal set-shifting abilities (Cavedini et al., 2010; Bradbury et al., 2011; Demeter et al., 2013) raising the hypothesis that perfectionistic personality traits could underpin both AN symptomatology and poor set-shifting abilities (Friederich and Herzog, 2011). From a clinical standpoint, such personality traits are of particular interest since associated with negative outcomes (Crane et al., 2007) and possible mediators in the treatment of AN (Lock et al., 2005).

This study aims to further understand the cognitive profile of set-shifting in AN. Adopting a methodology already used in the field (Roberts et al., 2010) we aim at identifying those clinical features and personality traits that could be associated with poor versus intact set-shifting.

Our a priori hypothesis was that poor set-shifting in AN could be associated with more severe perfectionistic personality traits, eating psychopathology and depressive symptoms, independently from nutritional status.

2. Methods

2.1. Patients and procedures

The study population consisted of 153 adult participants, 94 individuals diagnosed with AN, 78 restricting (AN-R) and 16 binge-purging (AN-BP) subtype and 59 healthy controls (HC). AN patients were both inpatients ($N=68$, 72%) and outpatients ($N=26$, 28%) consecutively recruited at the Eating Disorders Center of the San Giovanni Battista Hospital of the University of Turin, Italy, between February, 2010 and March, 2013. All participants provided written informed consent according to the ethical committee of the Department of Neuroscience of the University of Turin.

Patients were included in this study who met the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I) (First et al., 1997) diagnostic criteria for AN throughout the prior year. HC participants were recruited at the University of Turin through flyers. Exclusion criteria for both groups were a) male gender; b) IQ < 85 (as measured with the Wechsler Adult Intelligence Scale-Revised; Wechsler, 1997), c) active medical problems (i.e., epilepsy) or suicidal ideation; d) a history of serious head injury involving loss of consciousness; e) alcohol or substance abuse within 90 days of study participation as assessed per clinical interview. Moreover, none of the HC was on psychotropic medications or met criteria for a current or lifetime diagnosis of EDs or other Axis I disorders, as assessed by an experienced psychiatrist using the SCID-I. Participants were all Caucasian; all affected individuals completed the assessments in the first week of treatment to minimize confounders due to treatment interventions.

2.2. Measures

2.2.1. Psychiatric assessment

All participants were assessed using the following self-reported measures: Eating Disorder Inventory-2 (EDI-2; Garner, 1991), Beck Depression Inventory (BDI; Beck et al., 1961), and Temperament and Character Inventory (TCI; Cloninger et al., 1993). In addition, body mass index (BMI) for all participants was also measured.

The Beck Depression Inventory (BDI). The BDI (Beck et al., 1961) is a 13-item self-report questionnaire used to evaluate the severity of depressive symptoms. For people who have been clinically diagnosed, scores from 0 to 9 represent minimal depressive symptoms, scores of 10 to 16 indicate mild depression, scores of 17 to 29 indicate moderate depression and scores of 30 to 63 indicate severe depression. The BDI demonstrated high internal consistency, with alpha coefficients of 0.86 and 0.81 for psychiatric and non-psychiatric populations, respectively (Beck et al., 1988).

The Eating Disorder Inventory-2 (EDI-2). The EDI-2 (Garner, 1991) is a self-report inventory that measures disordered eating attitudes, behaviors and personality traits common to individuals diagnosed with an eating disorder. Eleven subscales evaluate symptoms and psychological correlates of the eating disorders with high scores reflecting pathology. A high level of internal consistency was found, indicated by Cronbach's alpha values between 0.82 and 0.93 (Thiel and Paul, 2006).

The Temperament and Character Inventory (TCI). The TCI (Cloninger et al., 1993) is a 240-item self-administered questionnaire divided into seven dimensions. Four of these dimensions assess temperament: novelty seeking (NS) expresses the level of explora-tory activity, harm avoidance (HA) reflects the efficiency of the behavioral inhibition system, reward dependence (RD) reflects the maintenance of rewarded behavior, and persistence (P) expresses maintenance of behavior as an indicator of frustration tolerance. The other three dimensions assess character: self-directedness (SD) expresses self-concepts about autonomy and integrity, cooperativeness (C) deals with self-concepts about others and the ability to cooperate, and self-transcendence (ST) expresses the relationship between the self and the external world as a whole. The TCI showed good properties as regards both internal consistency and test–retest reliability (Fossati et al., 2007).

2.2.2. Neuropsychological assessment

We used the Wisconsin Card Sorting Test pen–paper version (WCST, Berg, 1948; Heaton, 1981) with two card decks of 64 cards, to assess abstraction ability and cognitive strategies in response to changing environmental contingencies. We exam-ined (according to Laiacona et al., 2000) the following quantitative measures of the WCST: a) global score that represents an overall index of WCST performance and estimates how many cards the subject actually used in excess of the minimum necessary to achieve the six categories (global score = n of trials – [n of achieved categories × 10]), b) perseverative errors, that show participants' difficulties with changing categories of classification; this is a measure of cognitive inflexibility which specifically addresses individuals' tendency to perseverate; c) non-perseverative errors, namely a general score of errors not due to perseveration; and d) failure to maintain set, showing as to whether participants change criterion before testing driver indication; this score indicates a failure in comprehending test strategies. All partici-pants have been assessed by a clinical psychologist specifically trained to administer this neuropsychological assessment.

According to Roberts et al. (2010) we explored the cognitive profile of set-shifting ability in AN using a composite variable that divided the AN patients in three groups according to their level of set-shifting: poor, intact, and superior (for details, see section below).

2.3. Statistical analysis

The SPSS statistical software package was used for data analysis. As regards continuous variables (i.e., clinical data, neuropsychological tests, and question-naires), independent samples t-test and Mann–Whitney test were used to evaluate significant differences between AN individuals versus HC and AN-R versus AN-BP participants, respectively. For categorical variables, Fisher's exact test has been used to compare AN-R and AN-BP subgroups to maximize reliability independently of cell counts.

We split the sample into those with poor, intact or superior set-shifting abilities using the distribution of the current HC group. The global score at WCST was re-coded as follows: low if the score fell below 1 standard deviation (S.D.) of the HC mean, moderate if it fell within 1 S.D. either side of the mean, or high if it was greater than 1 S.D. above the HC mean (the variable was normally distributed in the HC group, task score varied in the direction: more errors = higher score). Indivi-duals showing high scores were re-coded as having poor set-shifting, those with low scores as superior set-shifting, and all the others as intact set-shifting.

Cohen's d effect sizes were calculated for the WSCT comparisons. Differences are defined as negligible (≥ -0.15 and < 0.15), small (≥ 0.15 and < 0.40), medium (≥ 0.40 and < 0.75), large (≥ 0.75 and < 1.10), very large (≥ 1.10 and < 1.45), and huge (> 1.45).

To check the influence of years of education, BMI and depressive symptoms (as measured by the BDI) on WCST performance of AN individuals versus HC, a univariate general linear model (UGLM) was used.

Fisher's exact test was used to investigate the distribution of inpatients versus outpatients and AN-R versus AN-BP subtypes across set-shifting groups. A one-way analysis of variance (ANOVA) with Bonferroni post-hoc was calculated to investigate clinical features and personality traits by set-shifting ability. To check the influence of personality dimensions or depression symptomatology on the three groups, a univariate general linear model (UGLM) was used. A level of significance of alpha < 0.05 was considered.

3. Results

3.1. Clinical and demographic features of the sample

We enrolled 94 AN patients and 59 HC. As shown in Table 1, AN patients showed a duration of illness of 7.13 ± 6.55 years.