Clinical investigation of set-shifting subtypes in anorexia nervosa.

(Article begins on next page)

25 September 2024

Clinical investigation of set-shifting subtypes in anorexia nervosa

Giovanni Abbate-Daga*, SaraBuzzichelli, EnricaMarzola, FedericoAmianto, SecondoFassino

Eating Disorders Center for Treatment and Research, Department of Neuroscience, University of Turin, Turin, Italy

*Corresponding author: Tel.: +39 011 6335196; fax: +39 011 6335749. E-mail address: giovanni.abbatedaga@unito.it

Abstract

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.

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 and Tchanturia et al., 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 and 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 and 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 and 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 and Lilenfeld, 2011). Additionally, a "maladaptive" profile (Krug et al., 2011) characterizes a subgroup of patients with low reward dependence. However, to date the influence of personality on neuropsychological performances 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 and 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 and 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 exploratory 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 and Heaton, 1981) with two card decks of 64 cards, to assess abstraction ability and cognitive strategies in response to changing environmental contingencies. We examined (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 $\times 10$]), 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 participants 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 questionnaires), 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). Individuals 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. The HC group did not differ from the AN group as regards age (AN=24.74±7.25 years; HC=25.08±3.23 years; Table 1) and IQ levels (104.12±13.06 versus 105.2±12.77, $t= -0.5$, $p>0.05$) whilst significant differences were found with respect to years of education (15.44±2.54 versus 12.39±2.89 years, respectively; $t= -6.63$; $p<0.001$) which was controlled for as a confounding variable in subsequent analyses.

Table 1. Demographic and clinical characteristics of the sample.

	AN (*N=94*)	HC (*N=59*)	*t*-test	*p*
Age	24.74 (±7.25)	25.08 (±3.23)	−0.34	0.735
Years of education	12.39 (±2.89)	15.44 (±2.55)	−6.63	**0.001**
BMI	15.17 (±1.98)	20.64 (±2.01)	−16.56	**0.001**
Duration of illness	7.13 (±6.56)	–	–	–
BDI	14.50 (±8.63)	2.90 (±3.61)	9.8	**0.001**
EDI-2				
DT	12.71 (±7.25)	1.37 (±2.79)	11.47	**0.001**
B	3.28 (±4.80)	0.66 (±1.72)	4.02	**0.001**
BD	13.52 (±6.75)	4.88 (±4.71)	8.59	**0.001**
I	11.21 (±8.09)	2.07 (±3.22)	8.28	**0.001**
P	5.79 (±4.05)	2.85 (±3.33)	4.67	**0.001**
ID	6.52 (±4.69)	1.63 (±2.43)	7.41	**0.001**
IA	9.81 (±7.43)	1.14 (±2.22)	8.71	**0.001**
MF	8.19 (±6.21)	3.88 (±3.93)	4.76	**0.001**
A	7.63 (±5.50)	2.59 (±2.41)	6.63	**0.001**
IR	6.13 (±6.13)	0.97 (±1.63)	6.32	**0.001**
SI	8.23 (±5.20)	2.58 (±2.95)	7.62	**0.001**
TCI				
NS	17.77 (±5.46)	20.44 (±6.66)	−2.71	**0.008**
HA	23.38 (±10.78)	18.51 (±11.94)	2.61	**0.010**
RD	15.24 (±3.74)	17.53 (±5.51)	−3.05	**0.003**
P	6.05 (±5.51)	6.05 (±6.69)	0.002	**0.998**
SD	23.67 (±9.30)	32.90 (±7.22)	−6.49	**0.001**
C	31.98 (±7.64)	35.19 (±5.01)	−2.86	**0.005**
ST	12.00 (±6.79)	12.53 (±7.64)	−0.44	**0.658**

Female anorexia nervosa (AN) patients and healthy controls (HC).

Mean and standard deviation are provided.

Statistically significant differences are shown in bold under *p* values.

BMI: body mass index; BDI: Beck Depression Inventory; EDI-2: Eating Disorder Inventory; DT: drive for thinness; B: bulimia; BD: body dissatisfaction; I: ineffectiveness; P: perfectionism; ID: interpersonal distrust; IA: interoceptive awareness; MF: maturity fears; A: asceticism; IR: impulse regulation; SI: social insecurity; TCI: Temperament and Character Inventory; NS: novelty seeking; HA: harm avoidance; RD: reward dependence; C: cooperativeness; SD: self-directedness; P: persistence; ST: self-transcendence.

AN individuals showed significantly lower BMI and higher BDI scores than HC and scored differently from HC on all EDI-2 subscales. AN individuals reported also (see Table 1). As regards personality traits, the AN group showed significantly lower novelty seeking, reward dependence, cooperativeness, and self-directedness but higher harm avoidance than HC (Table 1).

Although the AN-BP group (n=16) was not as large as the AN-R one (n=78), non-parametric tests showed no significant differences on BMI, BDI, and EDI-2 subscales between AN subtypes (p>0.05), with the only exception of the bulimia subscale on the EDI-2 that was significantly higher in the binge-purging subtype (AN-R=2.13±3.56; AN-BP=8.88±6.10; p<0.001).

3.2. Set-shifting ability

We did not find significant differences between AN-R and AN-BP patients as regards set-shifting (p>0.05, data not shown) whilst the differences between AN and HC on the WCST resulted significant: in fact, the AN group scored markedly higher than HC on all WCST measures, in particular global score (p<0.001) and non-perseverative errors (p<0.001; for further details see Table 2). When the differences between groups were corrected for years of education, BMI, and BDI all results remained significant (Table 2). A medium effect size was found for global score, non-perseverative errors and failure in maintaining the set, while a small effect size was reported for perseverative errors (Table 2).

Table 2. Neuropsychological profile on the Wisconsin Card Sorting Test (WCST) by group.

	AN	HC	Test statistics				Cohen′s Effect Size
	(N=94)	(N=59)	t-test		UGLM[a]		
			t	p	F (1,148)	p	
WCST							
Global score	25.99 (±21.90)	15.00 (±9.3)	3.65	**0.001**	5.79	**0.001**	0.61 (medium)
Perseverative errors	6.67 (±4.96)	5.27 (±2.58)	2	**0.047**	2.43	**0.050**	0.34 (small)
Non-perseverative errors	8.99 (±9.7)	4.78 (±2.42)	3.26	**0.001**	3.71	**0.007**	0.55 (medium)
Failure	0.68 (±1.38)	0.15 (±0.61)	2.77	**0.006**	3.29	**0.013**	0.47 (medium)

AN: anorexia nervosa; HC: healthy controls. Mean and standard deviation are provided and statistically significant differences are shown in bold under p values.

[a]Univariate general linear model corrected for BMI, BDI, and years of education.

After recoding the set-shifting performance of the AN group according to the aforementioned criteria, we found $n=30$ (31.9%) patients displaying poor set-shifting, $n=61$ (64.9%) intact set-shifting and only $n=3$ (3.2%) superior set-shifting. We included three individuals with superior set-shifting in the intact-set shifting group for statistical reasons. Therefore, two groups emerged: $n=64$ AN with intact and $n=30$ AN with poor set-shifting, homogeneously distributed between AN-R and AN-BP (Fisher′s exact test $p=0.77$).

The poor and intact set-shifting groups did not differ as regards proportion of inpatients (80% versus 70%, respectively, Fisher′s exact test $p=0.326$) nor duration of illness (8.27±7.28 versus 6.59±6.17 years, respectively, $t=-1.55$, $p=0.251$) nor IQ (data not shown).

Performing a one-way ANOVA with Bonferroni post-hoc, the three groups (AN with intact set-shifting, AN with poor set shifting, and HC) were found not to differ as regards age (see Table 3). Both groups of intact and poor set shifting differed from HC with respect to years of education and BMI whilst AN patients with intact or poor set-shifting reported homogeneous results on these measures.

Table 3. Demographic and clinical features by group.

	AN with intact set-shifting (*N*=64)	AN with poor set-shifting (*N*=30)	HC (*N*=59)	*F* (2,150)	*p*	**Bonferroni post-hoc**
Age	24.22 (±7.56)	25.87 (±6.53)	25.08 (±3.23)	1.548	0.216	**ANintact=ANpoor=HC**
Years of education	12.59 (±2.87)	11.97 (±2.94)	15.44 (±2.55)	21.526	**0.001**	**ANintact=ANpoor**; ANintact<HC; ANpoor<HC
BMI	15.34 (±2.03)	14.79 (±1.85)	20.65 (±2.01)	135.248	**0.001**	**ANintact=ANpoor**; ANintact<HC; ANpoor<HC
BDI	12.69 (±8.01)	20.17 (±8.07)	2.90 (±3.61)	68.334	**0.001**	**ANpoor>ANintact>HC**
EDI-2						
DT	12.30 (±7.25)	15.20 (±6.44)	1.37 (±2.79)	77.175	**0.001**	ANintact>HC; ANpoor>HC; ANpoor=ANintact
B	2.92 (±4.84)	4.72 (±5.01)	0.66 (±1.72)	10.712	**0.001**	ANintact>HC; ANpoor>HC; ANpoor=ANintact
BD	12.72 (±6.52)	16.40 (±6.66)	4.88 (±4.71)	43.672	**0.001**	ANintact>HC; ANpoor>HC; ANpoor=ANintact
I	10.07 (±7.05)	14.76 (±9.48)	2.07 (±3.22)	42.761	**0.001**	ANintact>HC; ANpoor>HC; ANpoor=ANintact
P	5.28 (±3.74)	7.48 (±4.63)	2.85 (±3.33)	14.780	**0.001**	ANintact>HC; ANpoor>HC; ANpoor=ANintact
ID	5.93 (±4.06)	8.16 (±5.63)	1.63 (±2.43)	32.098	**0.001**	ANintact>HC; ANpoor>HC; ANpoor=ANintact
IA	8.28 (±6.5)	14.00 (±8.01)	1.14 (±2.22)	53.357	**0.001**	**ANpoor>ANintact>HC**
MF	7.27 (±5.94)	11.44 (±6.51)	3.88 (±3.93)	18.487	**0.001**	**ANpoor>ANintact>HC**
A	7.22 (±5.16)	9.60 (±5.52)	2.59 (±2.41)	29.038	**0.001**	ANintact>HC; ANpoor>HC; ANpoor=ANintact
IR	5.07 (±5.21)	9.36 (±7.06)	0.97 (±1.63)	31.699	**0.001**	**ANpoor>ANintact>HC**
SI	7.73 (±4.75)	9.92 (±5.69)	2.58 (±2.95)	33.849	**0.001**	ANintact>HC; ANpoor>HC; ANpoor=ANintact
TCI						
NS	17.72 (±5.48)	19.44 (±5.12)	20.44 (±6.66)	3.168	**0.045**	ANintact=ANpoor=HC
HA	23.48 (±12.5)	23.76 (±6.9)	18.51 (±11.94)	3.375	**0.037**	ANintact=ANpoor=HC
RD	15.98 (±3.44)	13.76 (±3.88)	17.53 (±5.51)	6.379	**0.002**	**HC>ANpoor; HC=ANintact; ANpoor=ANintact**
P	6.43 (±6.77)	5.28 (±1.77)	6.05 (±6.69)	0.309	0.735	ANintact=ANpoor=HC
SD	24.62 (±8.88)	18.52 (±8.4)	32.90 (±7.22)	31.533	**0.001**	**HC>ANintact>ANpoor**
C	32.45 (±7.6)	30.04 (±8.15)	35.19 (±5.01)	5.636	**0.004**	**HC>ANpoor; HC=ANintact; ANpoor=ANintact**
ST	11.25 (±6.69)	13.80 (±7.39)	12.53 (±7.64)	1.195	0.306	ANintact=ANpoor=HC

Female anorexia nervosa (AN) patients with intact and poor set-shifting ability and healthy controls (HC).
Mean and standard deviation are provided.
Statistically significant differences are shown in bold under *p* values.
BDI: Beck Depression Inventory; EDI-2: Eating Disorder Inventory; DT: drive for thinness; B: bulimia; BD: body dissatisfaction; I: ineffectiveness; P: perfectionism; ID: interpersonal distrust; IA: interoceptive awareness; MF: maturity fears; A: asceticism; IR: impulse regulation; SI: social insecurity; TCI: Temperament and Character Inventory; NS: novelty seeking; HA: harm avoidance; RD: reward dependence; C: cooperativeness; SD: self-directedness; P: persistence; ST: self-transcendence.

Moreover, interoceptive awareness, impulse regulation and maturity fears subscales on the EDI-2 were significantly different among the three groups ($p<0.05$), whilst on all other subscales the AN group with poor set-shifting did not differ significantly from those with intact set-shifting (Table 3).

As regards depressive symptomatology, significant differences emerged among groups; in particular, AN individuals with poor set-shifting reported significantly higher BDI scores than those with intact set-shifting and both AN groups showed significant higher depressive symptomatology when compared to HC (Table 3).

With respect to personality, cooperativeness and reward dependence resulted significantly higher only in the HC versus AN poor set-shifting comparison while self-directedness differed significantly among all groups (Table 3).

When significant EDI-2 subscales were controlled for BDI, the differences among groups remained significant only as regards interoceptive awareness ($F=3.842$; d.f.=2, 149; $p<0.05$) while all differences remained significant in all groups when controlled for personality variables (interoceptive awareness: $F=17.849$; d.f.=2, 149; $p<0.001$; impulsivity: $F=10.085$; d.f.=2, 149; $p<0.001$; maturity fears: $F=3.103$; d.f.=2, 149; $p<0.05$). When we controlled the significant personality traits for BDI, none of the variables remained significant although reward dependence subscale showed a trend towards statistical significance ($F=2.405$; d.f.=2, 149; $p=0.094$).

4. Discussion

With this study we aimed at identifying poor versus intact set-shifting subtypes in AN with a specific focus on the investigation of the association between set-shifting abilities and clinical features and personality traits. Our findings are in line with previous literature showing that adults with AN report poor cognitive flexibility, independently from eating disorder subtype and BMI (Abbate-Daga et al., 2011, Tchanturia et al., 2011, Tchanturia et al., 2012 and Galimberti et al., 2013). However, cognitive changes do not occur in all affected individuals (Nakazato et al., 2010, Roberts et al., 2010, Konstantakopoulos et al., 2011 and Rose et al., 2012).

We split the sample into those with poor versus intact set-shifting to investigate the clinical features of each subtype. Our a priori hypothesis was only partially confirmed. As expected we found a difference in depressive symptoms between set-shifting groups but only interoceptive awareness as measured by the EDI-2 differed between intact versus poor set shifting group after controlling for depression. Moreover, perfectionistic traits, as measured by both EDI-2 (i.e., perfectionism subscale) and TCI (i.e., persistence subscale which is a broad construct including both perfectionism and the ability to maintain a non-remunerative behavior) did not differ between subtypes, differently from what we initially hypothesized. Still, reward dependence, differently from what we expected, showed a trend towards significance, even after controlling for depression.

Interestingly, those with poor set-shifting were significantly more depressed than those with intact set-shifting and HC. This is not in line with a large part of previous literature (Roberts et al., 2010) but it represents an interesting finding because depression has been recently shown to be involved in set-shifting performances (Abbate-Daga et al., 2011 and Giel et al., 2012). In fact, it is a common comorbid condition of AN as both full-blown diagnosis and clinical symptomatology (Abbate-Daga et al., 2011). Additionally, depressed patients are likely to report marked alterations of set-shifting abilities (Veiel, 1997, Austin et al., 2001 and Godard et al., 2011). Therefore, in line with other

authors (Giel et al., 2012), we propose the need for further investigations of this issue in the ongoing debate on neuropsychological features of AN individuals.

As regards eating psychopathology, we found that the poor set-shifting group reported overall higher scores on all EDI-2 subscales with interoceptive awareness (namely poorer interoceptive awareness), impulse regulation, and maturity fear reaching significance; however, after controlling for depression, only interoceptive awareness remained significant. Using the EDI-2 we confirmed previous literature highlighting no correlations between cognitive performances on the WCST and severity of eating psychopathology as measured by the Yale–Brown–Cornell scale for EDs (Roberts et al., 2010). Hence, poor set-shifting might represent a maladaptive coping strategy rather than a symptom-related thinking style.

This said, interoceptive awareness is a key psychological aspect of AN (Fassino et al., 2004 and Wagner et al., 2006) and it has been found to play a relevant role in several respects including AN pathogenesis (Skårderud, 2007). AN individuals tend to have an impaired recognition not only of visceral sensations but also of bodily signals (Pollatos et al., 2008). Accordingly, neurobiological research on AN proposed a link between difficulties in the recognition of homeostatic bodily needs and an exaggerated inhibition of those executive abilities involved in response to reward (Kaye et al., 2013). The correlation we found between poor interoceptive awareness and poor set-shifting ability seems to support the aforementioned literature and raises the speculative hypothesis of a link between bodily needs, enhanced behavioral inhibition, and neuropsychological functioning in AN.

Our previous work suggested that cognitive remediation therapy (CRT) can be effective in significantly modifying interoceptive awareness (Abbate-Daga et al., 2012). CRT showed promising results in helping patients to develop a more flexible thinking style also promoting a deeper insight into one′s own thinking processes (Davies and Tchanturia, 2005 and Tchanturia et al., 2008). Overall these data raise the possibility that the improvement in cognitive flexibility may be somehow related to those in interoceptive awareness.

We could not confirm our hypothesis as regards personality. From this study a lack of correlation between perfectionism and poor performance on the WCST emerged. Even though poor set-shifting does not characterize all individuals with perfectionistic traits (Pitt et al., 2010), future studies are needed to evaluate not only the global measures but also the multidimensionality (Bardone-Cone et al., 2007) of perfectionism.

However, we unexpectedly found that poor set-shifting subtype showed significantly lower reward dependence (RD) and cooperativeness (C) when compared to HC. In summary, those who were less responsive to reward and less cooperative showed worse performances than HC. These findings seem to support the role of socio-motivational factors in AN during set-shifting tasks, as already found in healthy individuals with studies reporting a link between goal values and perseverative errors (Hare et al., 2008 and Graham et al., 2009). However, poor motivation may be better explained by the depressive psychopathology rather than personality; future work should ensure whether a causal relationship can be found in this regard.

Reward dependence resulted related to depressive symptoms, in line with the approach-motivation deficits shown in depression (Henriques and Davidson, 2000 and Must et al., 2006) and bulimia nervosa (Galderisi et al., 2011). Notwithstanding the dearth of literature addressing the impact of reward on executive functions, the activation of reward circuits could be necessary to perform an effective set-shifting strategy during the WCST task (Graham et al., 2009).

Concluding, our findings highlight the complex interaction between cognitive performances and clinical features that could partially explain the wide variability of reported WCST performances in AN (Maddox et al., 2010) particularly as regards the role of depressive symptomatology and poor interoceptive awareness. Some limitations should be acknowledged: AN and HC groups differed as regards number of participants and years of education, the AN-BP subgroup was smaller than the AN-R one, and we used the WCST as only measure to split set-shifting groups and the cross-sectional design of this study makes it impossible to address causality. Further research is warranted to clarify these issues.

References

G. Abbate-Daga, S. Buzzichelli, F. Amianto, G. Rocca, E. Marzola, S.M. McClintock, S. Fassino. **Cognitive flexibility in verbal and nonverbal domains and decision making in anorexia nervosa patients: a pilot study.** BMC Psychiatry, 11 (2011), p. 162.

G. Abbate-Daga, S. Buzzichelli, E. Marzola, F. Amianto, S. Fassino. **Effectiveness of cognitive remediation therapy (CRT) in anorexia nervosa: a case series.** Journal of Clinical and Experimental Neuropsychology, 34 (10) (2012), pp. 1009–1015.

F. Amianto, G. Abbate-Daga, S. Morando, C. Sobrero, S. Fassino. **Personality development characteristics of women with anorexia nervosa, their healthy siblings and healthy controls: What prevents and what relates to psychopathology?.** Psychiatry Research, 187 (3) (2011), pp. 401–408.

M.P. Austin, P. Mitchell, G.M. Goodwin. **Cognitive deficits in depression: possible implications for functional neuropathology.** British Journal of Psychiatry, 178 (2001), pp. 200–206.

A.M. Bardone-Cone, S.A. Wonderlich, R.O. Frost, C.M. Bulik, J.E. Mitchell, S. Uppala, H. Simonich. **Perfectionism and eating disorders: current status and future directions.** Clinical Psychology Review, 27 (2007), pp. 384–405.

A.T. Beck, C.H. Ward, M. Mendelson, J. Mock, J. Erbaugh. **An inventory for measuring depression.** Archives of General Psychiatry, 4 (1961), pp. 561–571.

Beck, R. Steer, M. Garbin. **Psychometric properties of the beck depression inventory: twenty-five years of evaluation.** Clinical Psychology Review, 8 (1) (1988), pp. 77–100.

E.A. Berg. **A simple objective technique for measuring flexibility in thinking.** The Journal of General Psychology, 39 (1948), pp. 15–22.

C. Bradbury, S.E. Cassin, N.A. Rector. **Obsessive beliefs and neurocognitive flexibility in obsessive–compulsive disorder.** Psychiatry Research, 15 (187) (2011), pp. 160–165.

K. Bühren, V. Mainz, B. Herpertz-Dahlmann, K. Schäfer, B. Kahraman-Lanzerath, C. Lente, K. Konrad. **Cognitive flexibility in juvenile anorexia nervosa patients before and after weight recovery.** Journal of Neural Transmission, 119 (9) (2012), pp. 1047–1057.

S. Calderoni, F. Muratori, C. Leggero, A. Narzisi, F. Apicella, U. Balottin, T. Carigi, S. Maestro, F. Fabbro, C. Urgesi. **Neuropsychological functioning in children and adolescents with restrictive-type anorexia nervosa: an in-depth investigation with NEPSY-II.** Journal of Clinical and Experimental Neuropsychology, 35 (2) (2013), pp. 167–179.

P. Cavedini, C. Zorzi, M. Piccinni, M.C. Cavallini, L. Bellodi. **Executive dysfunctions in obsessive–compulsive patients and unaffected relatives: searching for a new intermediate phenotype.** Biological Psychiatry, 15 (67) (2010), pp. 1178–1184.

C.R. Cloninger, D.M. Svrakic, T.R. Przybeck. **A psychobiological model of temperament and character.** Archives of General Psychiatry, 50 (12) (1993), pp. 975–990.

M.K. Crane, H.R. Bogner, G.K. Brown, J.J. Gallo. **The link between depressive symptoms, negative cognitive bias and memory complaints in older adults.** Aging and Mental Health, 11 (6) (2007), pp. 708–715.

H. Davies, K. Tchanturia. **Cognitive remediation therapy as an intervention for acute anorexia nervosa: a case report.** European review of Eating Disorders, 13 (2005), pp. 311–316.

G. Demeter, M. Racsmány, K. Csigó, A. Harsányi, A. Németh, L. Döme. **Intact short-term memory and impaired executive functions in obsessive compulsive disorder.** Ideggyógyászati szemle, 30 (66) (2013), pp. 35–41.

S.J. Egan, T.D. Wade, R. Shafran. **Perfectionism as a transdiagnostic process: a clinical review.** Clinical Psychology Review, 31 (2011), pp. 203–212.

S. Fassino, A. Pierò, C. Gramaglia, G. Abbate-Daga. **Clinical, psychopathological and personality correlates of interoceptive awareness in anorexia nervosa, bulimia nervosa and obesity.** Psychopathology, 37 (2004), pp. 168–174.

J.R. Ferrari, W.T. Mautz. **Predicting perfectionism: applying tests of rigidity.** Journal of Clinical Psychology, 53 (1) (1997), pp. 1–6.

M.B. First, R.L. Spitzer, M. Gibbon, J.B.W. Williams. Structured Clinical Interview for DSM IV Axis I Disorders (SCID-I), Clinician Version, Administration Booklet, American Psychiatric Publishing, Washington, DC (1997).

Fossati, C.R. Cloninger, D. Villa, S. Borroni, F. Grazioli, L. Giarolli, M. Battaglia, C. Maffei. **Reliability and validity of the Italian version of the Temperament and Character Inventory-Revised in an outpatient sample.** Comprehensive Psychiatry, 48 (4) (2007), pp. 380–387.

H.C. Friederich, W. Herzog. **Cognitive-behavioral flexibility in anorexia nervosa.** Current Topics in Behavioral Neurosciences, 6 (2011), pp. 111–123.

S. Galderisi, P. Bucci, A. Mucci, L. Bellodi, G.B. Cassano, P. Santonastaso, S. Erzegovesi, A. Favaro, M. Mauri, P. Monteleone, M. Maj. **Neurocognitive functioning in bulimia nervosa: the role of neuroendocrine, personality and clinical aspects.** Psychological Medicine, 41 (4) (2011), pp. 839–848.

E. Galimberti, E. Fadda, M.C. Cavallini, R.M. Martoni, S. Erzegovesi, L. Bellodi. **Executive functioning in anorexia nervosa patients and their unaffected relatives.** Psychiatry Research, 208 (3) (2013), pp. 238–244.

E. Galimberti, R.M. Martoni, M.C. Cavallini, S. Erzegovesi, L. Bellodi. **Motor inhibition and cognitive flexibility in eating disorder subtypes.** Progress in Neuropsychopharmacology and Biological Psychiatry, 36 (2) (2012), pp. 307–312.

D. Garner. Eating Disorder Inventory 2: Professional Manual, Psychological Assessment Resources, Odessa (1991).

K.E. Giel, A. Wittorf, L. Wolkenstein, S. Klingberg, E. Drimmer, M. Schönenberg, A.M. Rapp, A.J. Fallgatter, M. Hautzinger, S. Zipfel. **Is impaired set-shifting a feature of "pure" anorexia nervosa? Investigating the role of depression in set-shifting ability in anorexia nervosa and unipolar depression.** Psychiatry Research, 200 (2–3) (2012), pp. 538–543.

J. Godard, S. Grondin, P. Baruch, M.F. Lafleur. **Psychosocial and neurocognitive profiles in depressed patients with major depressive disorder and bipolar disorder.** Psychiatry Research, 190 (2–3) (2011), pp. 244–252.

S. Graham, E. Phua, C.S. Soon, T. Oh, C. Au, B. Shuter, S.C. Wang, I.B. Yeh. **Role of medial cortical, hippocampal and striatal interactions during cognitive set-shifting.** Neuroimage, 45 (4) (2009), pp. 1359–1367.

T.A. Hare, J. O'Doherty, C.F. Camerer, W. Schultz, A. Rangel. **Dissociating the role of the orbitofrontal cortex and the striatum in the computation of goal values and prediction errors.** The Journal of Neuroscience, 28 (22) (2008), pp. 5623–5630.

K.R. Heaton. A Manual for Wisconsin Card Sorting Test, FI: P.E.A, Odessa (1981).

J.B. Henriques, R.J. Davidson. **Decreased responsiveness to reward in depression.** Cognition and Emotion, 14 (2000), pp. 711–714.

Jáuregui-Lobera. **Neuropsychology of eating disorders: 1995–2012.** Journal of Neuropsychiatric Disease and Treatment, 9 (2013), pp. 415–430.

W.H. Kaye, C.E. Wierenga, U.F. Bailer, A.N. Simmons, A. Wagner, A. Bischoff-Grethe. **Does a shared neurobiology for foods and drugs of abuse contribute to extremes of food ingestion in anorexia and bulimia nervosa?.** Biological Psychiatry, 73 (9) (2013), pp. 836–842.

P.K. Keel, K.J. Forney. **Psychosocial risk factors for eating disorders.** International Journal of Eating Disorders, 46 (2013), pp. 433–439.

G. Konstantakopoulos, K. Tchanturia, S.A. Surguladze, A.S. David. **Insight in eating disorders: clinical and cognitive correlates.** Psychological Medicine, 41 (9) (2011), pp. 1951–1961.

Krug, T. Root, C. Bulik, R. Granero, E. Penelo, S. Jiménez-Murcia, F. Fernández-Aranda. **Redefining phenotypes in eating disorders based on personality: a latent profile analysis.** Psychiatry Research, 188 (3) (2011), pp. 439–445.

M. Laiacona, M.G. Inzaghi, A. De Tanti, E. Capitani. **Wisconsin card sorting test: a new global score, with Italian norms, and its relationship with the Weigl sorting test.** Neurological Sciences, 21 (5) (2000), pp. 279–291.

L.R. Lilenfeld. **Personality and temperament.** Current Topics in Behavioural Neurosciences, 6 (2011), pp. 3–16.

Lock, W.S. Agras, S. Bryson, H.C. Kraemer. **A comparison of short- and long-term family therapy for adolescent anorexia nervosa.** Journal of the American Academy of Child and Adolescent Psychiatry, 44 (7) (2005), pp. 632–639.

W.T. Maddox, J.V. Filoteo, B.D. Glass, A.B. Markman. **Regulatory match effects on a modified Wisconsin Card Sort Task.** Journal of the International Neuropsychological Society, 16 (2) (2010), pp. 352–359.

Must, Z. Szabó, N. Bódi, A. Szász, Z. Janka, S. Kéri. **Sensitivity to reward and punishment and the prefrontal cortex in major depression.** Journal of Affective Disorders, 90 (2–3) (2006), pp. 209–215.

M. Nakazato, K. Hashimoto, U. Schmidt, K. Tchanturia, I.C. Campbell, D.A. Collier, M. Iyo, J. Treasure. **Serum glutamine, set-shifting ability and anorexia nervosa.** Annals of General Psychiatry, 9 (2010), p. 29.

K.M. O′Brien, N.K. Vincent. **Psychiatric comorbidity in anorexia and bulimia nervosa: nature, prevalence, and causal relationships.** Clinical Psychology Review, 23 (1) (2003), pp. 57–74.

R. Pignatti, V. Bernasconi. **Personality, clinical features, and test instructions can affect executive functions in Eating Disorders.** Eating Behaviours, 14 (2) (2013), pp. 233–236.

S. Pitt, R. Lewis, S. Morgan, D. Woodward. **Cognitive remediation therapy in an outpatient setting: a case series.** Eating and Weight Disorders, 15 (2010), pp. 281–286.

O. Pollatos, A.L. Kurz, J. Albrecht, T. Schreder, A.M. Kleemann, V. Schöpf, R. Kopietz, M. Wiesmann, R. Schandry. **Reduced perception of bodily signals in anorexia nervosa.** Eating Behaviours, 9 (4) (2008), pp. 381–388.

M.E. Roberts, K. Tchanturia, D. Stahl, L. Southgate, J. Treasure. **A systematic review and meta-analysis of set-shifting ability in eating disorders.** Psychological Medicine, 37 (8) (2007), pp. 1075–1084.

M.E. Roberts, K. Tchanturia, J.L. Treasure. **Exploring the neurocognitive signature of poor set-shifting in anorexia and bulimia nervosa.** Journal of Psychiatric Research, 44 (14) (2010), pp. 964–970.

M.E. Roberts, K. Tchanturia, J.L. Treasure. **Is attention to detail a similarly strong candidate endophenotype for anorexia nervosa and bulimia nervosa?.** The World Journal of Biological Psychiatry, 14 (6) (2013), pp. 452–463.

M. Rose, I. Frampton, B. Lask. **A case series investigating distinct neuropsychological profiles in children and adolescents with anorexia nervosa.** European Eating Disorders Review, 20 (1) (2012), pp. 32–38.

Sarrar, S. Ehrlich, J.V. Merle, E. Pfeiffer, U. Lehmkuhl, N. Schneider. **Cognitive flexibility and Agouti-related protein in adolescent patients with anorexia nervosa.** Psychoneuroendocrinology, 36 (9) (2011), pp. 1396–1406.

Y. Sato, N. Saito, A. Utsumi, E. Aizawa, T. Shoji, M. Izumiyama, H. Mushiake, M. Hongo, S. Fukudo. **Neural basis of impaired cognitive flexibility in patients with anorexia nervosa.** PLoS One, 8 (5) (2013), p. e61108.

D.L. Schrijvers, E.R. De Bruijn, M. Destoop, W. Hulstijn, B.G. Sabbe. **The impact of perfectionism and anxiety traits on action monitoring in major depressive disorder.** Journal of Neural Transmission, 117 (7) (2010), pp. 869–880.

F. Skårderud. **Eating one′s words, part I: 'Concretised metaphors' and reflective function in anorexia nervosa – an interview study.** European Eating Disorders Review, 15 (3) (2007), pp. 163–174.

.E. Steinglass, B.T. Walsh, Y. Stern. **Set shifting deficit in anorexia nervosa.** Journal of the International Neuropsychological Society, 12 (3) (2006), pp. 431–435.

Tchanturia, H. Davies, C. Lopez, U. Schmidt, J. Treasure, T. Wykes. **Neuropsychological task performance before and after cognitive remediation in anorexia nervosa: a pilot case-series.** Psychological Medicine, 38 (9) (2008), pp. 1371–1373.

Tchanturia, H. Davies, M. Roberts, A. Harrison, M. Nakazato, U. Schmidt, J. Treasure, R. Morris. **Poor cognitive flexibility in eating disorders: examining the evidence using the Wisconsin Card Sorting Task.** PLoS One, 7 (1) (2012), p. e28331.

Tchanturia, A. Harrison, H. Davies, M. Roberts, A. Oldershaw, M. Nakazato, D. Stahl, R. Morris, U. Schmidt, J. Treasure. **Cognitive flexibility and clinical severity in eating disorders.** PLoS One, 6 (6) (2011), p. e20462.

Thiel, T. Paul. **Test–retest reliability of the Eating Disorder Inventory 2.** Journal of Psychosomatic Research, 61 (4) (2006), pp. 567–569.

H.O. Veiel. **A preliminary profile of neuropsychological deficits associated with major depression.** Journal of Clinical and Experimental Neuropsychology, 19 (4) (1997), pp. 587–603.

Wagner, N.C. Barbarich-Marsteller, G.K. Frank, U.F. Bailer, S.A. Wonderlich, R.D. Crosby, S.E. Henry, V. Vogel, K. Plotnicov, C. McConaha, W.H. Kaye. **Personality traits after recovery from eating disorders: do subtypes differ?.** International Journal of Eating Disorders, 39 (4) (2006), pp. 276–284.

D. Wechsler. Wechsler Adult Intelligence Scale – Revised, Giunti O.S, Firenze, Italy (1997).

J. Yager, M.J. Delvin, K.A. Halmi, D.B. Herzog, A.J. Mitchell, P. Powers, K.J. Zerbe. **Guideline; Watch.** Practice Guideline for the Treatment of Patients With Eating Disorders, 3rd edition (2012).