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TITLE OF THE THESIS

Cold and Hot Cognition in Anorexia Nervosa: cognitive rigidity, perfectionism, interoceptive awareness and emotional competences

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1. Background

Eating Disorders (EDs) are complex and difficult-to-treat illnesses that are often chronic and disabling and are characterized by aberrant patterns of feeding behavior. Anorexia Nervosa (AN) is an ED characterized by an ego syntonic resistance to eating couples with severe weight loss due to a relentless pursuit of thinness and restrictive eating. Affected individuals are paradoxical observed with thoughts about food, despite a reduction in food intake. Even if emaciated, they perceive themselves as fat due to serious body image distortion. Two subtypes of eating-related behavior in AN have been defined. The first, restricting-type anorexics (R-AN) lose weight purely by dieting and exercising without binge eating or purging. The second, binge eating/purging-type anorexics (BP-AN), also restrict their food intake and exercise to lose weight, but they also periodically engage in binge eating and/or purging behaviors (DSM-5; APA,2013).

AN is a disorder of unknown etiology that most commonly begins during adolescence in women. Causes of AN are often considered to be complex with contributions from cultural pressures (Keel & Forney, 2013) as dieting and the pursuit of thinness are common in industrialized countries. Yet AN affects only an estimated 0.9% of females in the general population (Smink et al., 2012).

Pathogenesis of Eds is complex and, to date, only partially understood. It is presumed be influenced by developmental, social, and biological processes within the bio-psycho-social framework (Karwautz et al., 2011). Certainly, cultural attitudes toward standards of physical attractiveness have relevance, but it is unlikely that the preeminent influences in pathogenesis are sociocultural. Dieting behavior and a drive toward thinness are unusually common in industrialization countries throughout the word, yet AN affects less than 1% of women in the general population. Moreover, this syndrome has a relatively typical clinical presentation, sex distribution, ang age of onset, supporting the plausibility of intrinsic biological vulnerabilities (Kaye et al., 2013).

Such a disparity between the high prevalence of pressures for thinness and the low prevalence of AN combined with the stereotypic presentation, premorbid vulnerabilities developmentally specific age of onset, and gender distribution underscores the role of biological aspects with respect to vulnerabilities. Substantial evidence shows that genes contribute significantly to this regard, accounting for approximately 50% to 80% of the risk for developing AN (Bulik et al., 2006; Kaye et al., 2013; Bulik, 2016). The transmitted liability to AN may be mediated by a more diffused phenotype of continuous, heritable behavioral traits related to disordered eating regulation (Bulik et al., 2005; Klump, McGue, & Iacono, 2000), often resulting in subthreshold forms of ED in families (Lilenfeld et al., 1998; Strober et al., 2000).

Although currently unknown, in order to clarify the etiology of AN several neural systems have been called into question, including those associated with cognitive self-regulatory control, motivation/reward, and hunger regulation (Kaye et al., 2009; O'Hara et al., 2015). A conceptualization of models with a "top-down" (i.e., modulatory mechanisms underpinned by a prefrontal cognitive control) versus "bottom-up" (i.e., limbic and interoceptive processes) processing systems. This imbalance would entail the alteration of factors such as homeostatic need, responses to reward, and motivational drive (O'Hara et al., 2015). Several lines of research propose that in AN this hyper-activation of "top-down" systems predominates on "bottom-up" appetitive responses, as a consequence from an AN symptomatology point of view, this would lead to an aberrant desire to be thin, high anticipatory anxiety when exposed to eating, and behavioral rigidity including excessive control over food intake (Kaye et al., 2009).

However, within the bio-psycho-social framework (Fassino et al., 2010), accumulating evidence suggests that emotional disturbances are endemic to the AN field as well (Skarderud et al., 2007; Abbate-Daga et al., 2015). For example, high rates of co-occurring mood and anxiety disorders have been reported in AN (Kaye et al., 2004; Swinbourne and Touyz, 2007). Still, studies also suggest that AN is characterized by elevated negative emotionality like depressive symptoms, negative affect and affective states (Waller et al., 2003; Fassino et al., 2007; Abbate-Daga et al., 2012). Finally, personality traits like high arm avoidance (Fassino et al., 2002; Kaye et al., 2009) and/or other psychiatric disorders associated with disturbances in emotional functioning (e.g.,borderline personality disorder) are also common among individuals with AN (Sansone and Sansone, 2011; Phillipou et al., 2015).

Individuals with AN tend to be resistant to treatment (Marzola et al., 2012; Abbate-Daga et al., 2013) and deny having an illness. Moreover, many to most with AN continue to have some core symptoms after treatment, they might be considered to have some degree of treatment resistance (Marzola et al., 2012; Fassino & Abbate-Daga, 2013). Improvements in the understanding and treatment of Eds are of immense clinical and public health importance (NICE, 2004) since these are frequently chronic, relapsing illnesses (Steinhausen, 2002; Abbate-Daga et al., 2013; Walsh 2013) with substantial and costly medical morbidity (Westmoreland et al., 2016).

Importantly, for AN, there is no proven treatment that reverses symptoms (NICE, 2004); as a consequence, it has the highest death rate of any psychiatric illness (Papadopoulos et al., 2009). Individuals with AN often go to great lengths to keep their disorder a secret to avoid treatment and maintain the pathological behavior meant to control their weight and body image (Vitousek et al., 1998). Unwillingness to seek treatment is a hallmark of this disorder and has relevant effect on treatment outcome. In fact, a substantial number of ill individuals do not seek treatment (Neubauer

et al., 2014). Illness often becomes apparent only when patients become emaciated from gradually losing weight.

The process of recovery in AN is poorly understood and, in most cases, protracted. Still, approximately 50% to 70% of affected individuals will eventually have complete or moderate resolution of the illness, often in the early to mid-20s (Steinhausen, 2002; Wagner et al., 2006).

To enhance treatment motivation and to overcome treatment resistance, pathogenetic and maintenance factors should be better understood, treatments should be focused on maintenance factors and symptomatic trigger, in particular in acute stage, to allow patients to gradually abandon symptomatic behaviors and built a good therapeutic alliance favored by a good motivation to change (Marzola et al., 2019).

Literature about risk and maintenance factors is broad, it is accepted that perfectionism is involved in onset and maintenance of AN (Coulbert et al., 2015; Anderluh et al., 2003), this personality traits could also be clinically associated with cognitive rigidity that has been proposed as endophenotype for AN (Talbot et al., 2015). Also, Childhood obsessive-compulsive personality traits have been demonstrated to represent medium potency risk factors for the development of a ED (Anderluh et al., 2003; Jacobi et al., 2004). Similarly, Harm Avoidance, characterized by cautiousness, anxiety and inhibition, has been proposed as potential risk factor for EDs (Lilenfeld et al., 2011) and, linked with the intolerance to uncertainty could be involved in symptoms maintenance mechanism. Intolerance to uncertainty seems to be also associated with Alexithymia (Abbate-Daga et al., 2015) that is considered hallmark for ED (Fassino et al., 2007; Abbate-Daga et al., 2013). Another trait that may be involved in AN psychopathology is poor Interoceptive Awareness (Lilenfeld et al., 2006; Duffy et al., 2019), that is represented by an impaired recognition of both emotional states and hunger and satiety and it is often a core psychopathological element of the EDs (Fassino et al., 2004).

Looking at the whole of data should be possible consider two macro factors: Cold cognition and the rigidity aspects with the link to personality traits like perfectionism and Hot cognition characterized by all emotional problems, alexithymia, emotional regulation and his link with Interoceptive Awareness problems. These fields needed deeper investigation to better understand psychotogenic mechanism of AN and improve treatment outcomes.

The aim of my PhD Project was thus to contribute to exploring psychopathological mechanism and maintenance factors of AN and their clinical implications, focusing on:

a) Cold cognition, with the aim to confirm the literature about cognitive flexibility impairment in Anorexia Nervosa (AN) patients and further examine the relationship between neuropsychological rigidity and perfectionism.

[This study has been published in 2018 in European Eating Disorders Review, with the title: *Cognitive Rigidity and Perfectionism in Anorexia Nervosa: Is there an association?* Authors were: Buzzichelli S., Marzola E., Amianto F., Fassino S., Abbate-Daga G.]

b) Hot cognition, with the aim to investigate interoceptive accuracy (IAc) and awareness (IA) in Anorexia Nervosa patients, and the relationship with eating disorders psychopathology, depression, anxiety and emotional intelligence.

[This study is in preparation for publication]

2. Cognitive rigidity and Perfectionism in Anorexia Nervosa

Perfectionism and cognitive rigidity in anorexia nervosa: Is there an association?

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Abstract

Little is known about the relationship between neuropsychology, personality, and eating psychopathology in anorexia nervosa (AN). We aimed to investigate the interaction between set shifting and perfectionism in AN and to ascertain the role of perfectionism as a mediator between set shifting and eating psychopathology. Eighty-five patients with AN and 71 healthy controls completed Eating Disorder Inventory-2 (using 8 as a cut-off for generating groups with high vs. low perfectionism), Beck Depression Inventory, Wisconsin Card Sorting Test, Trail Making Task, and Hayling Sentence Completion Task. Our findings support heightened cognitive inflexibility in individuals with AN, particularly in those with high perfectionism. Perfectionism resulted to be a mediator of the relationship between a measure of set shifting and drive for thinness, but this finding did not remain significant when including in the model only those with AN. Taken together, these data suggest a complex and nonexclusive association between set shifting, eating psychopathology, and perfectionism.

KEYWORDS
anorexia nervosa, cognitive rigidity, eating disorders, perfectionism, set shifting

2.1 Introduction

Several studies explored the possibility that cognitive rigidity could be an endophenotype of anorexia nervosa (AN; Talbot, et al., 2015), a complex mental illness whose pathogenesis is largely unknown (Brockmeyer, Friederich, & Schmidt, 2017). Set-shifting has been investigated as an endophenotype also because AN patients consistently showed inefficient and stable set-shifting abilities (Abbate-Daga et al., 2011; Tchanturia et al., 2012; Abbate-Daga, Buzzichelli, Marzola, Amianto & Fassino, 2014; Aloi et al., 2015; Westwood, Stahl, Mandy & Tchanturia, 2016). Also personality has been investigated to better understand AN pathogenesis; among personality traits, perfectionism resulted strongly associated with eating disorders (EDs) as both risk and maintaining factor (Egan, Wade & Shafran, 2011). With more detail, evidence consistently showed self-reported and performance-based perfectionism as heightened in individuals with EDs (Tchanturia et al., 2014; Lloyd, Yiend, Schmidt & Tchanturia, 2014). Interestingly, research showed perfectionism not only as correlated with drive for thinness (DT) in patients with AN, but also as preceding eating psychopathology in AN (Halmi et al., 2012).

Little is known about the relationship between set-shifting and personality. Theoretically, rigidity, inhibition, and perfectionism could be linked to difficulties in executive functions. Parallels between perfectionism and set-shifting are common in clinical practice and have been already hypothesized in literature (Schmidt & Treasure, 2006). Furthermore, retrospective research showed set-shifting as associated with childhood perfectionism (Tchanturia et al., 2004); therefore, perfectionism could influence AN patients' thinking style and problem solving abilities thus partially influencing their neuropsychological performances.

The interaction between neuropsychological performance and perfectionism in AN received scant attention and mixed findings are available. In a recent study, higher personal standards (Frost, Marten, Lahart & Rosenblate, 1990) were associated with better Trial Making Test scores in both affected and non-affected individuals (Vall & Wade, 2015). In another study higher personal standards were found to be correlated with good set-shifting in recovered AN patients and with poor set-shifting in healthy controls (Lindner, Fichter & Quadflieg, 2014). Buhren and collaborators (2012) found a correlation between greater accuracy on neuropsychological test and perfectionism in young AN patients. In contrast, other studies highlighted the need for clarifying the interactions between perfectionism and set-shifting (Pignatti & Bernasconi, 2013) and no significant correlations between these constructs have been reported as well (Friederich et al., 2012). The available evidence is overall unsatisfactory also because previous studies used different measures of set-shifting, also without investigating verbal domains.

In order to bridge the aforementioned gaps in literature, this study has the following goals: a) to analyze the set-shifting performance concerning verbal and non-verbal domains across subsamples of AN patients and healthy controls (HCs) grouped according to their degrees of perfectionism; b) to ascertain the role of perfectionism as a mediator between cognitive rigidity and eating psychopathology, in particular DT. When designing this study we hypothesized to find: a) a relationship between suboptimal neuropsychological performance and perfectionism; b) perfectionism as mediator of the link between cognitive rigidity and eating psychopathology.

2.2 Materials and methods

2.2.1 Participants

The sample consisted of 156 adult female participants, 85 individuals diagnosed with AN restricting subtype (RAN) and 71 healthy controls (HCs). AN patients were consecutively recruited at the Eating Disorders Center of University of Turin, Italy. All participants provided written informed consent according to the ethical committee of University of Turin. Patients were included in this study who met criteria for AN according to DSM-5 (American Psychiatric Association, 2013), HCs were recruited at the University of Turin through flyers. Exclusion criteria for the entire sample are the following: a) male gender; b) Wechsler Adult Intelligence Scale-Revised Intellectual Quotient < 85 (Wechsler, 1997); c) history of cranial trauma with loss of consciousness; d) alcohol or substance dependence or abuse; e) medical problems; f) suicidal ideation. Moreover, none of the HCs was on psychotropic medications or met criteria for a current or lifetime diagnosis of EDs or other mental disorders, as clinically assessed by an experienced psychiatrist. Participants were all Caucasian, all affected individuals completed the assessment in the first week of treatment to minimize treatment-related confounders.

2.2.2 Measures and procedure

All participants were assessed using self-reported measures: Eating Disorders Inventory-2 (EDI-2; Garner, 1991) to evaluate eating psychopathology and Beck Depression Inventory (BDI; Beck et al., 1961) to assess depression. Participants' weight and high were measured by a trained nurse to calculate body mass index (BMI). Perfectionism was measured with the perfectionism sub-scale of the EDI-2, and we set the cut off at 8 according to the EDI-2 manual instructions (Garner, 1991, Garner, Rizzardi, Trombini, Trombini, 1995). Three groups emerged: RAN High Perfectionism (RAN-HP; n=21), RAN Low Perfectionism (RAN-LP; n=64) and HCs with low perfectionism scores (n=64). Seven individuals in the HCs group were outliers and thus excluded.

To evaluate cognitive flexibility we used the following pen and paper neuropsychological tests: Wisconsin Card Sorting Test (WCST; Berg, 1948; Heaton, 1981), Trail Making Task (TMTA-B; Reitan, 1958) and the Hayling Sentence Completion task (HSCT; Burgess & Shallice, 1997).

2.2.3 Statistical analysis

The SPSS 24.0 statistical software package (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp) has been used for data analysis. Sample t-test has been run to evaluate significant differences between RAN versus HCs. A Chi Square analysis has been used to evaluate the distribution of perfectionism score between RAN and HCs groups. To check clinical differences between RAN-HP and RAN-LP a t-test has been used. A one way ANOVA with Bonferroni post-hoc analysis evaluated differences between RAN-HP, RAN-LP, and HCs.

Linear regression analyses were used to: a) explore the eventual independent associations between cognitive rigidity and both perfectionism and DT; b) verify the possible association between perfectionism and DT. Multivariate regression analysis and the Sobel test (Baron & Kenny, 1986) were then used in order to ascertain the mediation role of perfectionism. Perfect mediation holds if the independent variable has no effect when the mediator is controlled for (Baron & Kenny, 1986). The amount of mediation is usually called the "indirect effect" (Figure 1).

2.3 Results

2.3.1 Demographics and clinical features of the sample

The sample was composed of 156 individuals, 85 were RAN and 71 HCs. Those with RAN were inpatients with mean duration of illness of 6.2 years (SD=6.4) and mean BMI of 15.1 (SD=1, 9). RAN and HCs groups were matched for age but not for years of education ($p<0.001$): in fact, RAN individuals resulted as less educated probably because of the impact of AN on social and school functioning. As expected, RAN had lower BMI ($p<0.001$), higher scores on the EDI-2 ($p<0.001$), and higher depressive symptoms as measured by the BDI ($p<0.001$) than HCs. See Table 1 for details.

2.3.2 Neuropsychological performances

As shown in Table 1, the RAN group performed significantly worse than HCs on all WCST subscales: global score, perseverations, non-perseverative errors, and failure in maintaining set, showing significant difficulties in set-shifting.

Regarding the TMT score, both time scores, part A and B were significantly higher in RAN patients when compared to HCs; in contrast, no significant differences were found in the number of errors in part B (Table 1).

RAN individuals performed significantly worse on the HSCT with both net score and reaction time significantly higher than those of HCs ($p<0.001$ and $p<0.05$, respectively; Table 1). Poor score coupled with high reaction time indicate major impairments to finding an efficient flexible strategy.

Table 1. Demographic, clinical and neuropsychological assessment of the sample.

		RAN (n=85) Mean(SD)	HCs (n=71) Mean(SD)	*Test statistics* t	*p*
Age, years		23.73 (6.68)	24.82 (3.09)	-1.263	0.209
Years of education		11.99 (2.97)	15.52 (2.67)	-7.735	0.001**
Body Mass Index		15.06 (1.89)	20.82 (2.19)	-17.618	0.001**
Duration of illness		6.24 (6.37)	-	-	-
EDI-2	DT	12.54 (7.24)	2.07 (3.97)	10.886	0.001**
	B	2.07 (3.46)	1.01 (2.38)	2.176	0.031*
	BD	13.34 (6.76)	5.48 (5.41)	7.912	0.001**
BDI		13.77 (7.85)	3.12 (3.77)	10.446	0.001**
HSCT	Net Score	3.58 (2.60)	2.32 (1.97)	3.331	0.001**
	Reaction time A	0.502 (0.238)	0.389 (0.233)	2.967	0.003*
	Reaction time B	2.110 (1.632)	1.518 (1.130)	2.570	0.011*
TMT	Time A	40.69 (15.53)	34.05 (9.27)	3.162	0.002*
	Time B	79.12 (31.64)	64.42 (17.24)	3.504	0.001**
	Time B-A	39.28 (26.23)	30.52 (15.10)	2.489	0.014*
	Errors part B	0.28 (0.64)	0.17 (0.41)	1.247	0.214
WCST	Global Score	26.40 (21.14)	16.77 (11.49)	3.434	0.001**
	Perseverations	6.42 (5.01)	4.62 (2.89)	2.686	0.008*
	No perseverative errors	10.07 (10.09)	6.61 (6.32)	2.510	0.013*
	Failure	0.62 (1.32)	0.17 (0.61)	2.676	0.008*

* $p<0.05$, ** $p<0.001$

Legend: RAN: restricting type anorexia nervosa; HCs: healthy controls; BMI: Body Mass Index; BDI: Beck Depression Inventory; EDI-2: Eating Disorders Inventory-2; DT: drive for thinness; B: bulimia; BD: body dissatisfaction; WCST: Wisconsin Card Sorting Test; HSCT: Hayling Sentence Completion Task; TMT: Trail Making Test.

2.3.3 Neuropsychological performances across perfectionism groups

Within the RAN group, 21 (24.7%) individuals had high perfectionism scores (RAN-HP) and 64 (75.3%) had low perfectionism scores (RAN-LP); within the HCs group 7 individuals (9.9%) reported high perfectionism while the majority of this group (n=64, 90.1%) had low perfectionism scores. The distribution of high perfectionism scores significantly differed between RAN and HCs ($p=0.013$). Also in this light, HCs with high perfectionism have been considered as outliers and excluded from subsequent analysis.

Between RAN-HP and RAN-LP no significant differences were found in BMI, and years of education but RAN-HP showed a significantly longer duration of illness, more severe eating and depressive symptoms (Table 1).

With respect to the differences in neuropsychological performances across perfectionism groups (Table 2), RAN-LP and RAN-HP performed significantly worse than HCs on the WCST global score although the differences between RAN groups did not reach statistical significance. Perseverative errors did not significantly differ across groups; in contrast, RAN-HP differed from HCs in non-perseverative errors. Although not statistically significant, RAN-LP were found to have intermediate scores between RAN-HP and HCs with respect to non-perseverative errors. Finally, HCs reported a significantly lower number of failures than both AN groups which did not differ from each other.

Time A on the TMT resulted significantly lower for HCs when compared to RAN-LP. Time B resulted significantly lower in HCs when compared to both RAN groups also, RAN-HP showed greater scores than RAN-LP but the differences between RAN groups showed only a trend toward statistical significance. Similarly, the score time B-A was significantly higher in RAN-HP than HCs, with RAN-LP scoring an intermediate value; however, only the difference between RAN-HP and RAN-LP reached significance (Table 2).

Concerning the HSCT, the net score resulted significantly higher in RAN-HP when compared to HCs. The net score of RAN-LP was intermediate between those of RAN-HP and HCs although not reaching statistically significance (Table 2).

Table 2. Neuropsychological performance across groups comparing patients with anorexia nervosa with high versus low perfectionism and healthy controls.

		RAN-HP (n=21)	RAN-LP (n=64)	HCs (n=64)	Test statistics		
		Mean(SD)	Mean(SD)	Mean(SD)	F	*p*	Bonferroni post-hoc
HSCT	Net Score	4.05 (2.99)	3.42 (2.46)	2.45 (2.02)	4.662	0.011*	RAN-HP>HC
	Reaction time A	0.508 (0.141)	0.501 (0.263)	0.399 (0.235)	3.354	0.055	-
	Reaction time B	1.850 (1.358)	2.193 (1.711)	1.563 (1.152)	3.017	0.052	-
TMT	Time A	41.90 (13.61)	40.29 (16.19)	34.05 (9.38)	4.685	0.011*	RAN-LP>HC
	Time B	88.95 (39.56)	75.90 (28.20)	64.40 (17.73)	7.650	0.001**	RAN-HP>HC RAN-LP>HC
	Time B-A	50.47 (31.65)	35.61 (23.31)	30.53 (15.45)	6.617	0.002*	RAN-HP>AN-LP RAN-HP>HC
	Errors part B	0.33 (0.79)	0.27 (0.59)	0.17 (0.45)	0.784	0.459	-
WCST	Global Score	27.19 (21.53)	26.14 (21.18)	17.09 (12.01)	4.978	0.008*	RAN-HP>HC RAN-LP>HC
	Perseverations	6.00 (4.75)	6.56 (5.11)	4.77 (2.93)	2.916	0.057	-
	No perseverative errors	12.67 (16.35)	9.22 (6.92)	6.69 (6.63)	3.974	0.021*	RAN-HP>HC
	Failure	0.52 (0.98)	0.66 (1.42)	0.17 (0.63)	3.302	0.040*	RAN-LP>HC

* $p<0.05$, ** $p<0.001$

Legend: RAN-HP: restricting type anorexia nervosa with high perfectionism; RAN-LP: restricting type anorexia nervosa with low perfectionism; HCs: healthy controls; WCST: Wisconsin Card Sorting Test; HSCT: Hayling Sentence Completion Task; TMT: Trail Making Test.

2.3.4 Mediation model

In order to run the mediation model we used the whole sample, only excluding those outliers (7 HCs reporting high perfectionism) that had already been excluded from previous analyses. As a proxy for cognitive rigidity we chose to carry on in the mediation model those indices of cognitive rigidity that significantly differed across groups of perfectionism (Table 2), namely TMT A, TMT B, TMT B-A, WCST global score, WCST non perseverative errors, WCST failures, and HSCT net score. As a first step, as shown in Table 3, we investigated the association between cognitive rigidity and DT finding that TMT B, TMT B-A, and WCST non perseverative errors resulted as significantly associated with DT (p= 0.024; p=0.027; p=0.015, respectively). Secondly, we tested the effect of cognitive rigidity on perfectionism reporting that TMT A, TMT B, and HSCT net score were significantly associated with perfectionism (p=0.016; p=0.017; p=0.005, respectively). Lastly, we found a significant association between perfectionism and DT (p=0.001). Among cognitive rigidity indices, only TMT B was significantly associated with both DT and perfectionism (p= 0.024 and p=0.017, respectively), so we used TMT B to run the mediation model. TMT B was significantly associated to DT but, when controlling for perfectionism, such

an association did not hold significance (Table 3) thus supporting perfectionism as a mediator of the relationship between cognitive rigidity and DT. The Sobel test confirmed this finding (Sobel test p= 0.031; Figure 1).

When including only the AN sample in the mediation model the association between cognitive rigidity and both DT and perfectionism was no longer significant (data not shown) while the association between perfectionism and DT remained significant (p=0.001).

Table 3. Linear regressions of the unmediated and mediated model investigating the relationship between set-shifting and drive for thinness

		DT	
		F (1,148)	*p*
HSCT	Net Score	3.781	0.054
TMT	Time A	2.660	0.105
	Time B	5.166	0.024*
	Time B-A	4.966	0.027*
WCST	Global Score	3.732	0.055
	No perseverative errors	6.061	0.015*
	Failure	1.690	0.196
TMT	Time B[§]	27.384	0.230

* p<0.05

[§]After correcting the model for perfectionism.

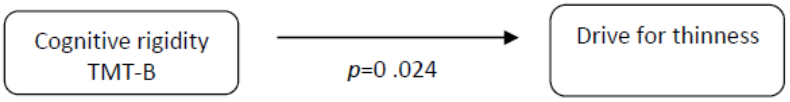
Legend: DT: drive for thinness; WCST: Wisconsin Card Sorting Test; HSCT: Hayling Sentence Completion Task; TMT: Trail Making Test.

As a first step, as shown in Table 3, we investigated the association between cognitive rigidity and DT finding that TMT B, TMT B-A, and WCST non-perseverative errors resulted as significantly associated with DT (p= 0.024; p=0.027; p=0.015, respectively). Secondly, we tested the effect of cognitive rigidity on perfectionism reporting that TMT A, TMT B, and HSCT net score were significantly associated with perfectionism (p=0.016; p=0.017; p=0.005, respectively). Lastly, we found a significant association between perfectionism and DT (p=0.001). Among cognitive rigidity indices, only TMT B was significantly associated with both DT and perfectionism (p= 0.024 and p=0.017, respectively), so we used TMT B to run the mediation model. TMT B was significantly associated to DT but, when controlling for perfectionism, such an association was no longer significant (Table 3) thus supporting perfectionism as a mediator of the relationship between cognitive rigidity and DT. The Sobel test confirmed this finding (Sobel test p= 0.031; Figure 1).

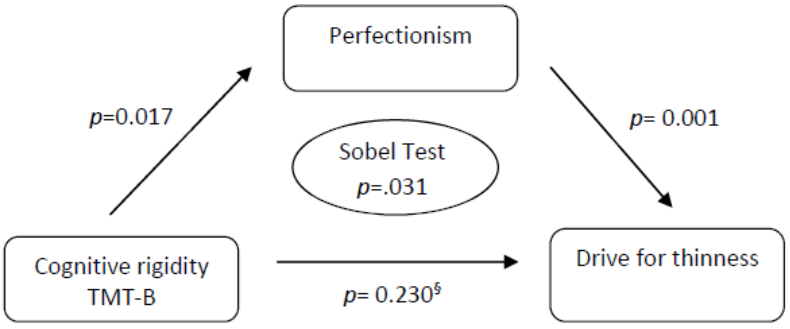
When including only the AN sample in the mediation model the association between cognitive rigidity and both DT and perfectionism was no longer significant (data not shown) while the association between perfectionism and DT remained significant (p=0.001).

Figure 1. Mediation model

A) Unmediated model



B) Mediated model



Representation of the mediation model. A) The direct effect of cognitive rigidity on drive for thinness is represented, B) The mediator role of perfectionism is shown and Sobel Test is given.

§After correcting the model for perfectionism.

2.4 Discussion

Data showed cognitive rigidity to be heightened in AN; moreover, a sort of gradient of severity across patients with high perfectionism, those with low perfectionism, and healthy controls emerged with regard to participants' neuropsychological performance. Also, perfectionism resulted to be a significant mediator of the relationship between set-shifting and eating psychopathology (i.e., drive for thinness) when TMT B was considered as a proxy for cognitive rigidity; nevertheless, this finding did not hold true when only patients with AN were included in the same mediation model.

In line with the a priori hypothesis, we found a relationship between neuropsychological performance and perfectionism; in fact, on one hand our data on set-shifting are overall in line with previous literature (Abbate-Daga et al., 2011, 2014; Talbot et al., 2015) but on the other hand we observed those with high perfectionism reporting the most marked inefficiencies in cognitive rigidity, when compared to patients with low perfectionism and HCs. This clear trend emerged, although the differences between patients with high versus low perfectionism did not reach statistical significance in all comparisons. Although novel, this finding is consistent with every-day clinical observations; in fact, marked perfectionism characterises only a subgroup of patients with AN and it is deemed to have an only partial impact on sufferers' neuropsychological performance (Vall & Wade, 2015; Pignatti & Bernasconi, 2013; Lindner et al., 2014).

Patients with different levels of perfectionism differed on the majority of the neuropsychological tests performed but not all, providing support to a multifaceted interaction between cognitive rigidity and perfectionism, as expected when designing this study. With more detail, all AN patients scored poorly on perseverative errors of the WCST, while non-perseverative errors resulted more linked to perfectionism. This finding is in line with previous literature showing perfectionism as influencing negatively recovered individuals' performance of set shifting, as measured by the Berg's Card Sorting Test (Lindner et al., 2014). On the TMT, Time A was higher not only in RAN-LP but also in RAN-HP when compared to HCs even if the latter difference did not hold significance when performing the post-hoc test, probably because of the difference in sample size of the two groups. Moreover, RAN-HP resulted significantly slower than RAN-LP on the TMT Time B-A; this finding is interesting as Time B-A represents specifically the time required to perform cognitive set-shifting without considering the time required to perform the control task (Time A) which asks participants to merge the numbers in ascending order. RAN-HP showed significantly longer shifting time than RAN-LP, thus indicating greater difficulty in applying an effective and flexible strategy in cognitive shifting with perfectionism potentially complicating and slowing down RAN patients' set-shifting ability.

Our findings are not in line with previous research (Val & Wade, 2015) reporting an association between TMT scores and perfectionism in an opposite direction: in fact, that study found high personal standards as associated with better cognitive flexibility. These conflicting data might be explained by the different measure used to assess perfectionism; in fact, clinical perfectionism (as measured by the EDI-2) could have a pejorative role on cognitive flexibility while high personal standards might be interpreted as enhancing cognitive performance.

Similarly, also verbal domains of cognitive rigidity seemed to be partially linked with perfectionism; in fact, even though statistical significance was not reached, HSCT net score was

higher in RAN-HP than in RAN-LP. This is a novel finding because very few studies investigated the verbal domains of cognitive rigidity (Abbate-Daga et al., 2011; Pignatti & Bernasconi, 2013). From a clinical point of view, RAN-HP and RAN-LP differed in duration of illness and eating psychopathology but not in BMI. According to these findings, perfectionism resulted indeed unrelated to the state of malnutrition but rather to AN patients' history and severity. This is consistent with data proposing perfectionism as maintaining factor in AN (Fairburn, Shafran & Cooper, 1999; Schmidt & Treasure, 2006; Lilenfeld, 2011); relatedly, it could potentially increase severity and duration of this disorder (Pignatti & Bernasconi, 2013). Still, recent research on healthy adolescents showed how perfectionism, when coupled to high body dissatisfaction, can be associated to high level of eating disorders symptoms (Boone et al., 2014).

We also aimed to investigate the role of perfectionism as a possible mediator of the association between cognitive rigidity and drive for thinness. This hypothesis was raised because our data showed that cognitive rigidity was associated to both perfectionism and eating psychopathology; moreover, perfectionism and drive for thinness were related to each other as well. This hypothesis was then confirmed when the relationship between cognitive rigidity and DT was controlled for perfectionism, such an association did not remain significant. However, as expected, a complex relationship between cognitive rigidity and perfectionism and eating psychopathology emerged and caution is required when analyzing this mediation model because of two main reasons. First, among cognitive rigidity indices, only TMT B resulted to mediate this association; although TMT B is a sound measure of set-shifting this model requires further replications. Also, some measures and not others could be associated with a multidimensional construct like perfectionism. Second, the mediation effect resulted significant when considering the whole sample (Sobel test $p=0.031$) but not if only individuals with AN were carried on into the analysis. Considering only patients with AN, perfectionism was significantly associated with DT but set-shifting was unrelated to both DT and perfectionism. On one hand, the sample size could partially explain this discrepancy so studies with more power are needed. However, on the other hand, other factors could be called into question when commenting this finding. In fact, cognitive rigidity is considered a precursor of perfectionism and a risk factor for eating disorders (Fairburn et al., 1999; Lilenfeld, Wonderlich, Riso, Crosby & Mitchell, 2006); notwithstanding, perfectionism would seem to play a partially independent role in the acute stage of AN. In fact, in currently ill individuals, perfectionism seems to become an independent maintenance factor significantly impacting on AN symptom severity. All in all, the data highlight the complex role of cognitive rigidity and perfectionism in eating disorder psychopathology. Therefore, perfectionism could mediate cognitive rigidity with respect to only some aspects of eating psychopathology,

According to our findings, set-shifting and perfectionism resulted to be related factors; this is in line with clinical observations since their association commonly characterizes patients with AN. However, the mediation role of perfectionism should be targeted by future studies. In fact, earlier studies (Tchanturia, Morris, Anderluh, Collier, Nikolaou et al., 2004) found in AN that cognitive rigidity was associated with childhood perfectionism but not with perfectionism in adulthood. Similarly to our findings on the AN sample, when eating psychopathology is taken into account, perfectionism and cognitive rigidity seem to have an independent role. In real-world clinical practice, those AN patients with greater cognitive inflexibility are likely to be in turn more perfectionistic; also, such a rigid aspects tend to impact on eating psychopathology as well. Even though this is a fairly common observation in every-day clinical practice, these findings show that the relationship between inflexibility, perfectionism, and eating psychopathology is more complicated than it seems and further research is needed to clarify it, maybe also including recovered individuals.

When analyzing these data, some limitations should be borne in mind: first and foremost, perfectionism has been assessed with a unidimensional scale while other instruments could be more detailed in describing perfectionism in a multidimensional way. also, other factors (e.g., anxiety symptoms) could be taken into account when investigating perfectionism and eating psychopathology. Finally a larger sample would be preferable and AN patients and HCs are not matched with respect to years of education.

Nevertheless, these findings provide new insights into AN psychopathology, namely a complex association between neuropsychological characteristics and perfectionism traits; in fact our findings support a role for perfectionism as mediator of the relationship between set-shifting and DT. However, according to a subset of our analysis, an independent role of cognitive rigidity and perfectionism cannot be ruled out in AN; in fact, in AN perfectionism failed to explain the association between other measures of set shifting and eating symptoms. Other studies are needed to better investigate the role of perfectionism, with a larger sample and potentially recruiting participants with high perfectionism without eating disorders. It would also be interesting to use a multidimensional scale (e.g., Frost Multidimensional perfectionism Scale; Frost et al., 1990), to analyse the role of depression also in regard to perfectionism as well as performance anxiety.

In closing, we found RAN-HP, RAN-LP, and HCs as distributed along a sort of severity gradient with respect to their neuropsychological performance even though on some tests the differences between RAN-HP and RAN-LP did not reach statistical significance. Although preliminary, these data suggest a complex and non-exclusive association between set-shifting, eating psychopathology, and perfectionism with the latter having a potential mediation role. In this light,

it can be raised the hypothesis that both cognitive rigidity and perfectionism can modulate AN severity with intertwined effects. Perfectionism should be taken into account in designing care protocols, Tchanturia, Larsson & Adamson (2016) have, in this regard, put into place a group treatment aimed at addressing perfectionism issues that would result to be effective in reducing clinical perfectionism. However, since patients with neuropsychological inefficiencies, high perfectionism, longer duration of illness, and severe eating disorders symptoms are commonly found, further research is needed to clarify the peculiarity of this clinical subgroup in AN.

3. Interoceptive Awareness and Emotional Intelligence in Anorexia Nervosa

3.1 Introduction

Interoception is the body-to-brain axis of sensation concerning the state of the internal body and its visceral organs (Cameron, 2001; Sherrington, 1948). We all perceive feelings from our body which provide a sense of our physiological condition, this is related to the basic fact that we "have" a body; that is, that we are "embodied" (Herbert et al., 2012). This is in accordance with the ''somatic marker'' hypothesis of Damasio (1994, 1999) stating that this meta-representation of bodily states constitutes an emotional feeling, accessible to consciousness and providing the ''gut-feeling'' that guides our decision processes and forms the basis for our ''self'' and consciousness.
Interoception consist of two aspects: Interoception Accuracy (IAc), that is the ability to detect and perceive body signals and internal states, and Interoceptive Awareness (IA) the aptitude to direct attention correctly on internal states and body signals and interpret them in emotional way, as a message about how I feal. The combination of these dimensions provides the sense of one's physical self and play a crucial role in emotional processing (Craig, 2002). Many theories of emotions suggest that bodily experience is a core component for encoding all emotional feelings (Craig 2009; Damasio 1999; Northoff, 2012).
Research on interoception of the cardiovascular (Critchely, et al., 2004; Herbert, Pollatos, & Shandry, 2007; Pollatos, Shandry, Aurer & Kaufmann, 2007; Shandry, 1981) and the gastrointestinal system (Stephan et al., 2003) and from pain research (Hosoi et al., 2010) underscores that there are significant interindividual differences in interoceptive accuracy and awareness. Interestingly Herbert et al., (2012) found that short term fasting intensifies IAc in healthy women; moreover, data in healthy women showed independence between IAc and IA but a partial association between IA and emotional susceptibility (Calì et al., 2015).
Eating disorders are complex psychiatric illness with unpredictable outcome and unknown etiopathogenesis (Halmi, 2005). Literature suggest that patients with AN showed difficulty in the perception of bodily signals (Kaye et al., 2009) and that Interoceptive Awareness play an important role in the pathogenesis of eating disorders including onset, maintenance and illness symptomatology (Fassino et al., 2004; Brown et al., 2017). A recent study (Marzola et al., 2019) found that altered IA is one of the premorbid factors found in Eating Disorders together with harm avoidance, social phobia, alexithymia and food obsessions.
Emotional recognition and regulation deficits are also considered core in eating disorders psychopathology, in this field the literature is extensive and consonant (Abbate Daga et al., 2015;

Zysberg, 2013). Disturbances in emotion processes are considerate candidate biological marker for Anorexia Nervosa (Hatch et al., 2010).

During the last decade, literature has been concentrated on the investigation of IAc and IA in Eating disorders: Pollatos et al (2008) found significantly lower IAc and IA in AN in comparison with HCs, another study found significantly lower IA but not IAc in AN than in HCs (Eshkevari et al., 2014). In contrast Khalsa et al. (2015) found significantly higher IAc in AN than in HCs. Moreover, an inverse correlation between IA and eating disorders psychopathology was found in AN (Brown et al., 2017). Literature underline also an association between IA and alexithymia (Pollatos et al., 2008) and emotional dysregulation (Eshekevary et al., 2014) in AN, but data are still poor and not comparable.

Literature about IAc and IA in AN is discordant and incomplete and the question about the link between IAc and IA and Emotional Competences in AN is still open.

The aims of this paper are a) to investigate IAc and IA in AN in comparison with HCs; b) explore the interaction between IAc and IA with eating disorders psychopathology and Emotional Competences in AN.

To evaluate IAc we used the most widely used in both AN patients and healthy people: the Heart-beat counting method by Shandry (1981), that consist on the heart-beat perception and the individual sensitivity for cardiac signals, in these tasks, participants are instructed to perceive their own heartbeats without feeling for their pulse. They allow calculating individual heartbeat scores that characterize the deviation of the subjectively felt cardiac signal from the objective cardiac signal, that is, the individual heartbeats.

To investigate IA we chose the Multidimensional Assessment of Interoceptive Awareness (MAIA; Mehling et al., 2012) that is a complete multidimensional scale of body signals perception, attention regulation on them and the awareness of the emotional meaning of body signals. The complexity of this measure allows us to better evaluate the differences between AN and HCs and the relationship with Eating disorders psychopathology and Emotional Competences measured with the multidimensional Profile of Emotional Competences (PEC; Brasseur & Mikolajczak, 2013). Previous literature did also support the use of MAIA in Eating disorders patients (Brown et al., 2017)

The a priori hypotheses were: a) found a significantly lower level of both IAc and IA in AN patients in comparison with HCs; b) found inverse associations between Interoception and AN symptomatology and a direct association between Interoception and Emotional Competences in both AN and healthy women.

3.2 Materials and methods

3.2.1 Participants

The clinical sample consisted in 67 eligible candidates consecutively recruited at the Eating Disorders Unit at the University of Turin, Italy, between October 2016 and December 2018. Inclusion criteria were: a) diagnosis of Anorexia Nervosa (AN) (both subtypes) as assessed with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)(First, 2015); b) female gender; c) age ranging from 16 to 40; d) no psychotic spectrum disorders.

Healthy Controls (HCs) were recruited at the same institution and in the same period through flyers; a total of 59 HCs was enrolled. HCs were excluded if using psychotropic medications or meeting criteria for a current or lifetime diagnosis of EDs or other mental disorders, as assessed by an experienced psychiatrist.

All participants were Caucasian, their height and weight were measured by a trained nurse, these measures were then used to calculate their body mass index (BMI, expressed as kg/m2).

This study was approved by the Ethics Committee of the Department of Neuroscience of the University of Turin, Italy. Written informed consent was obtained by all participants, and their parents for those who were minors.

3.2.2 Measures and procedure

All participants were asked to complete the following battery of assessments:

1) Eating Disorders Inventory-2 (EDI-2; Garner, 1991) the Italian version of a 91 items self-report questionnaire that provides measure of clinical characteristics of eating disorders in 11 subscales. For this study has been used only the first 3 subscales: Drive for Thinness (DT), Bulimia (BU) and Body Dissatisfaction (BD).

2) Beck Depression Inventory (BDI; Beck et al., 1961): the validated Italian version (Baggio et al., 1997) of a 13-item self-report questionnaire used to measure self-report depressive symptoms.

3) State and Trait Anxiety Inventory (STAI; Spielberger et al., 1983): the validated Italian version (Lazzari, Pancheri, 1980) of a 20 item instrument to self-report state anxiety, a temporary condition experienced in specific situations, and trait anxiety, a general tendency to perceive situations as threatening.

4) Multidimensional assessment of Interoceptive Awareness (MAIA; Mehling, 2012): the validated Italian version (Calì et al., 2015) of 32 items that provide measures of the awareness of body sensations (noticing subscale), the emotional reaction and attentional response to sensations (not distracting and not worrying subscales), the capacity to regulate attention (attention regulation subscales), the awareness of mind-body integrations (emotional awareness, self-regulation and body listening subscales) and trusting in body sensations (trusting subscale); a total scare was also calculated as a global index of interoceptive awareness (IA).

5) Profile of emotional Competence (PEC; Brasseur and Mikolajczak, 2013): the Italian version of 50 items to self-report the ability in identifying, expressing, understanding, regulating, and using emotions in both intrapersonal and interpersonal field.

Concluded the self-report assessment all participant performed the interoceptive accuracy (IAc) task according to the Heart Beat Counting Method (Shandry, 1981): IAc was assessed during electrocardiography, during a certain time of interval, between onset and offset of soft tone, presented by loudspeaker, the subject was to count her heart beats by concentrating on bodily feelings, possibly associated with the action of the heart. The subject was instructed not to take her own pulse or to try any other physical manipulations which might facilitate the detection of the heartbeat. The task was performed 3 times for time intervals lasting 25, 35, and 45 sec respectively, before starting and between the counting intervals, 30 sec of relaxing were granted. After the end of each time interval the subject was requested to report the counted number of heart beats.

3.2.3 Statistical analysis

The SPSS V26 statistical software package (IBM SPSS Statistics for Windows, Version V26 Armonk, NY: IBM Corp) was used for all analysis. Descriptive statistics were used to describe the sample, the Independent Sample t-test has been run to evaluate significant differences between Anorexia Nervosa Restrictive subtype (RAN) patients and Anorexia Nervosa Binge Purging Subtype (BPAN) patients and between AN and HCs. Cohen d effect sizes were calculated.

Cluster analysis, a combination of hierarchical and k-means ones, was performed to classify participants according to interoceptive awareness and emotional competence scores. Firstly, we conducted hierarchical cluster analysis on patients group to decide the number of clusters to adopt: we used the process of tree cutting, which consists in cutting the dendrogram (i.e., hierarchical analysis output showing the process of clusterization organized in branches) at the stage where the cluster coefficients start to rise exponentially, and then we applied the formula [number of cases – number of stages = number of clusters]. Then k-means cluster analysis was run introducing the number of clusters detected by the previous analysis also for the HCs group to make study

homogenous. K-means enables to create a new categorical variable which assigns each subject to a cluster; this variable was used for the following analysis. Independent-sample t-test was run to evaluate differences in eating disorders, depression and anxiety symptoms and emotional competences throw the two groups emerged from cluster analysis (good and low interoception). Finaly, log-linear regression was run to evaluate association between interoception and emotional competences and the case/control variable.

3.3 Results

3.3.1 Demographics and clinical features of the sample

The clinical sample was composed of 67 AN in-patient, 55 RAN and 12 BPAN. Since no significant differences were found between RAN and BPAN with the exception of the Bulimia subscale of EDI-2 and BMI, data attributable to the main clinical difference between the two subgroups, we considered, for further analysis, only one clinical group of AN patients.
AN resulted significantly younger and with less years of education than HCs; from a clinical point of view HCs had significantly lower scores in EDI-2, BDI and STAI tests and had significantly higher BMI, as expected (see Table 1).

Table 1 Demographics and clinical features of the sample

		AN (n=67)	HCs (n=59)	*Test statistics*		*Cohen's Effect Size*
		Mean(SD)	Mean(SD)	T	*P*	
Age, years		22.70 (7.09)	25.18 (2.67)	2.559	0.012*	Medium
Years of education		13.33 (2.79)	15.73 (2.31)	5.294	0.001**	Large
Body Mass Index		13.28 (1.94)	20.54 (1.43)	23.886	0.001**	Huge
Duration of illness		4.81 (6.08)	-	-	-	-
EDI-2	DT	13.51 (6.34)	2.98 (4.75)	-10.483	0.001**	Huge
	B	2.76 (4.50)	1.33 (2.29)	-2.213	0.029*	Medium
	BD	14.57 (6.78)	7.37 (7.01)	-5.878	0.001**	Large
BDI		14.75 (7.21)	3.25 (3.96)	-10.708	0.001**	Huge
STAI	State	53.94 (15.13)	37.52 (11.21)	-6.866	0.001**	Very Large
	Trait	59.15 (12.02)	42.73 (10.60)	-8.099	0.001**	Huge

* p<0.05, ** p<0.001

Legend: AN: anorexia nervosa; HCs: healthy controls; BDI: Beck Depression Inventory; EDI-2: Eating Disorders Inventory-2; DT: drive for thinness; B: bulimia; BD: body dissatisfaction; STAI: state and Trait Anxiety Inventory.

3.3.2 Interoceptive sensitivity and awareness

As shown in Table 2, the MAIA questionnaire showed AN patient as having significantly poorer IA than HCs. When compared to HCs, patients with AN were found to regulate the attention on body signals less well, not to listen to and trust them, and not to regulate themselves according to them.

However, regarding the perception of the body signals, no significant differences emerged between AN and HCs groups neither on the MAIA subscale noticing nor in the Heartbeat counting method.

Table 2 Intecoceptive Awareness

		AN (n=67) Mean(SD)	HCs (n=59) Mean(SD)	*Test statistics* t	*P*	*Cohen's Effect Size*
MAIA	Noticing	3.14(1.01)	3.37 (0.91)	1.364	0.175	-
	Not Distracting	2.31 (1.00)	2.29 (0.67)	-0.88	0.930	-
	Not Worrying	2.42 (1.26)	2.65 (0.96)	1.123	0.263	-
	Attention Regulation	2.45 (0.99)	3.22 (0.82)	4.756	0.001**	Large
	Emotional Awareness	3.18 (1.20)	3.45 (0.94)	1.355	0.178	-
	Self Regulation	1.54 (1.13)	2.66 (1.11)	5.629	0.001**	Large
	Body Listening	1.66 (1.17)	2.60 (0.99)	4.858	0.001**	Large
	Trusting	1.55 (1.32)	3.32 (1.05)	8.291	0.001**	Huge
	Total	2.36 (0.65)	3.06 (0.73)	5.692	0.001**	Large
HEARTBEAT COUNTING		0.59 (0.27)	0.56 (0.23)	-0.425	0.672	-

* p<0.05, ** p<0.001

Legend: AN: restricting type anorexia nervosa; HCs: healthy controls; MAIA: Multidimensional Assenssment of Interoceptive Awareness.

3.3.3 Emotional competences

Data showed that the AN group reported a significantly lower level of emotional competence both in intrapersonal and interpersonal areas (see Table 3), only the subscales Interpersonal utilization showed superimposable data in AN and HCs groups.

3.3.4 Cluster analysis

Table 3 Emotional Competence

		AN (n=67) Mean(SD)	HC (n=59) Mean(SD)	*Test statistics* t	*p*	*Cohen's Effect Size*
PEC	Intrapersonal Identification	2.74 (0.85)	3.81 (0.74)	7.108	0.001**	Very Large
	Interpersonal Identification	3.79 (0.66)	4.21 (0.56)	3.638	0.001**	Medium
	Intrapersonal Expression	2.76 (0.79)	3.52 (0.78)	5.202	0.001**	Large
	Interpersonal Expression	3.77 (0.71)	4.34 (0.49)	4.915	0.001**	Large
	Intrapersonal Understanding	2.81 (0.87)	3.93 (0.70)	7.549	0.001**	Very Large
	Interpersonal Understanding	3.31 (0.80)	4.03 (0.49)	5.868	0.001**	Large
	Intrapersonal Regulation	2.15 (0.76)	2.93 (0.82)	5.256	0.001**	Large
	Interpersonal Regulation	3.17 (0.88)	3.56 (0.58)	2.803	0.006*	Medium
	Intrapersonal Utilization	3.02 (0.81)	3.85 (0.62)	6.115	0.001**	Very Large
	Interpersonal Utilization	2.53 (0.95)	2.81 (0.76)	1.829	0.70	-
	Intrapersonal Total	2.70 (0.59)	3.61 (0.51)	8.724	0.001**	Huge
	Interpersonal Total	3.29 (0.62)	3.79 (0.44)	4.975	0.001**	Large
	Total	3.00 (0.47)	3.70 (0.43)	8.207	0.001**	Huge

* p<0.05, ** p<0.001

Legend: AN: anorexia nervosa; HCs: healthy controls; PEC: Profile of Emotional Competences.

AN patient

We run the hierarchical cluster analysis for patients, and we cut the dendrogram on at stage 65; then we applied [number of cases – number of stages = number of clusters] as it follows: 67-65 = 2.

K-means analysis classified patients homogeneously across the two clusters (Table 4): good (48%) and low (52%), Interoception. Only Heart-beat counting score and Not distracting and Not worrying (subscales of MAIA) did not result significant in clustering process.

Table 4. Final cluster of interoceptive sensitivity and awareness for patients with AN

	Inpatients with AN (n=67)		
	Low Interoception (n= 32)	**Good interoception (n= 35)**	**ANOVA *p***
Heart Beat Counting	0.54	0.64	0.131
MAIA			
Noticing	2.79	3.57	**0.001**
Not Distracting	2.27	2.28	0.958
Not Worrying	2.48	2.48	0.985
Attention Regulation	1.90	2.94	**0.000**
Emotional Awareness	2.33	3.95	**0.000**
Self Regulation	0.74	2.31	**0.000**
Body Listening	0.99	2.31	**0.000**
Trusting	0.80	2.21	**0.000**
Total	1.83	2.87	**0.000**

* p<0.05, ** p<0.001

Legend: AN: anorexia nervosa; MAIA: Multidimensional Assessment of Interoceptive Awareness.

T-test (Table 5) showed significant differences between AN low and good interoception in eating related, depressive and anxiety symptoms, no significant differences were found for BMI, age, years of illness.

AN patient with low Interoception had higher score in drive for thinness (subscale of EDI-2), BDI and state anxiety, and lower score in emotional competence (PEC).

Table 5. Psychopathology and emotional intelligence across AN Low and Good interoception groups.

		AN low Interoception (n=32) Mean(SD)	AN good interoception (n=35) Mean(SD)	*Test statistics* t	*p*
	Age	21.69 (6.43)	24 (7.74)	-1.32	0.190
	Years of education	13.28 (2.57)	13.37 (3.06)	-0.130	0.897
	Duration of illness	4.77 (6.94)	5.19 (5.46)	-0.276	0.783
	BMI	13.501 (2.18)	13.12(1.71)	0.818	0.416
EDI	Drive for thinness	15.22 (5.54)	12.09 (6.45)	2.094	**0.040**
	Bulimia	2.88 (4.86)	2.73 (4.32)	0.130	0.897
	Body dissatisfaction	15.88 (6.82)	13.58 (6.76)	1.368	0.176
BDI		16.92 (6.41)	12.82 (7.53)	2.361	**0.021**
STAI	State	57.87 (13.39)	50.24 (15.99)	2.062	**0.043**
	Trait	61.87 (11.19)	56.97(12.45)	1.652	0.104
PEC	Total	2.79 (0.45)	3.16 (0.46)	-3.203	**0.002**

* $p<0.05$, ** $p<0.001$

Legend: AN: anorexia nervosa; BMI: Body Mass Index; BDI: Beck Depression Inventory; EDI-2: Eating Disorders Inventory-2; STAI: State and Trait Anxiety Inventory; PEC: Profile of Emotional Competences.

HCs

K-means cluster analysis classified HCs in two clusters (Table 6), that showed the same trend in Interoception: good (58%) and low (42%). As for AN patient's Heart-beat counting score, not distracting and Not worrying (subscales of MAIA) did not result significant in clustering process. No significant differences were found in Age, years of education and BMI between good and low Interoception, HCs with low Interoception showed higher score in bulimia and body dissatisfaction (subscales of EDI), higher level of depression and anxiety and lower score in emotional competence (see Table 7).

Table 6. Final cluster of interoceptive sensitivity and awareness for HCs

	HCs (n=59)		
	Low Interoception (n= 25)	**Good interoception (n= 34)**	**ANOVA** *p*
Heart-Beat Counting	0.57	0.56	0.892
MAIA			
Noticing	2.71	3.86	**0.000**
Not Distracting	2.20	2.34	0.428
Not Worrying	2.64	2.65	0.967
Attention Regulation	2.66	3.60	**0.000**
Emotional Awareness	2.92	3.85	**0.000**
Self Regulation	1.81	3.25	**0.000**
Body Listening	1.79	3.18	**0.000**
Trusting	2.48	3.92	**0.000**
Total	2.45	3.42	**0.000**

* p<0.05, ** p<0.001

Legend: HCs: Healty Controls; MAIA: Multidimensional Assessment of Interoceptive Awareness.

Table 7. Psychopathology and emotional intelligence across HCs Low and Good interoception groups.

		HCs low Interoception (n=25) Mean(SD)	**HCs good interoception (n=34)** Mean(SD)	*Test statistics* t	*p*
	Age	25.56 (2.74)	24.91 (2.27)	-0.912	0.366
	Years of education	16.00 (2.18)	15.47 (2.40)	-0.869	0.388
	BMI	20.42 (1.45)	20.56 (1.40)	0.388	0.700
EDI	Drive for thinness	2.96 (4.35)	2.79 (5.00)	-0.133	0.895
	Bulimia	1.92 (2.83)	0.76 (1.52)	-2.022	**0.048**
	Body dissatisfaction	10.44 (7.59)	5.00 (5.73)	-3.140	**0.003**
BDI		4.84 (4.78)	2.53 (3.01)	-2.272	**0.027**
STAI	State	42.28 (11.48)	34.28 (11.48)	-2.895	**0.005**
	Trait	47.56 (9.84)	39.62 (9.81)	-3.069	**0.003**
PEC	Total	3.42 (0.36)	3.89 (0.68)	4.922	**0.000**

* p<0.05, ** p<0.001

Legend: HCs: Healty Controls; BMI: Body Mass Index; BDI: Beck Depression Inventory; EDI-2: Eating Disorders Inventory-2; STAI: State and Trait Anxiety Inventory; PEC: Profile of Emotional Competences.

3.3.5 Regression analysis

Log-linear regression was run including Heart-Beat Counting Method score, MAIA total score and PEC total score as Independent variables and AN vs HCs as dependent variable.

No significant association was found between IAc (heart-beat counting method score) and the case/control variable (B=0.315; p=0.682).

Significant association was found between IA (MAIA Total score) and case/control variable (B=-1.645; p<0.001), the association remain significant after controlling for age (B=-1.578; p<0.001)and years of education (B=-1.612; p<0.001) separately and together (B=-1.689; p<0.001).

Significant association war also found between emotional competence (Pec Total score) and case/control variable (B=-3.277; p<0.001), the association remain significant after controlling for age (B=-3.206; p<0.001)and years of education (B=-2.947; p<0.001) separately and together (B=-2.970; p<0.001).

3.4 Discussion

The aims of the study were to investigate IAc and IA in AN in comparison with HCs and to examine associations between Interoception and eating disorders psychopatology and emotional competences.

In contrast with the a priori hypothesis data showed similar IAc performance at the heart-beat counting method in patients with AN and HCs. Data about IA was instead in line with expectations, AN patient showed a significantly lower level of IA that HCs. MAIA is a complex and multidimensional instrument so could be worthwhile analyze all subscales in detail. The first subscale is noticing and it refers to the ability to detect and be aware of body signals, it is somehow an index of IAc rather than IA, our data showed no significant differences between AN and HCs groups in line with data about Heart Beat counting method. The second and the third subscale are about the tendency to not ignore and not worry about body signals perceived, our data showed that patients with AN had similar tendency of HCs in these subscales. The fourth subscale is attention regulation, patients with AN showed a significantly lower ability to sustain and control attention to body sensations in comparison with HCs even if the awareness of the connection between body sensations and emotional states (fifth subscale) results similar in AN and HCs groups. Lastly, patients with AN showed a significantly lower ability to regulate psychological distress by attention to body sensations (sixth subscale), significantly lower tendency to actively listen to the body (seventh subscale) and significantly lower level of trusting in body sensations (eighth

subscales). Reassuming these data, AN patients seems to correctly detect body signals and tendency to not distracting and not worrying with body sensations, but they are not able to sustain and control attention to body sensations even if they know that they are linked with emotional states. AN patient seems not to be able to use in emotional way, actively listening to and trusting body sensations correctly perceived. Previous literature about Interoceptive Accuracy and Awareness is controverse. In line with our data, with a comparable methodology, Eshekevari et al.,2014 found no significant differences between HCs and ED (AN and BN group) in IAc but significantly lower IA for ED group, instead Pollatos et al., 2008 found that AN had significantly lower IAc and IA in comparison with HCs. Klabunde et al., 2013 found that deficit in interoceptive sensitivity are present in individuals recovered from Bulimia nervosa, thus differences in IAc across diagnosis should be considered. An interesting paper by Khalsa et al., 2015 found abnormal visceral activation during intravenous infusion of caloric meal but a normal IAc ability for AN patients, even if the methodology is different, this is in line with our data. Could be possible to speculate that patients with AN had altered interoceptive predictor signals (Kaye et al., 2009; 2011), a good IAc ability in detects this visceral sensations (Khalsa et al., 2015), but significant difficulties to confer emotional significance to body sensations that lead to the deficits in emotional recognition and regulation that is a core of AN (Beadle et al., 2013; Abbate Daga et al., 2015; Harrison et al., 2009) and confirmed with present data about the significantly lower level of emotional competences found in PEC subscales in AN in comparison with HC groups.

The PEC reveals that AN patients are significantly impaired in both Intrapersonal and Interpersonal dimensions, they found difficulties in managing their own emotions and other's emotions in a relational context. The emotional profile that appeared for AN patients is characterized by poor ability in identify emotions, low expression of emotions in a social appropriate way and thus inadequate capacity in regulating stress and emotions. AN patients seems to be not brilliant in understanding causes and consequences of emotions and in using emotions to reflect about decisions and actions. Interesting AN patients had comparable scores in Interpersonal Utilization subscale, AN patients refers to be able to use emotions in relational context even if they do not identify emotions adequately.

These data are in line with previous literature that identify deficit in emotional regulation and alexithymia as hallmarks of anorexia nervosa psychopatology (Abbate Daga et al., 2015; Zysberg, 2013; Hatch et al., 2010; Adenzato et al., 2012). To our knowledge, to date, no data are available of PEC in AN in comparison with HCs, only a recent study (Doba et al., 2020) found that intrapersonal emotional competence mediate the relationship between insecure attachment and emotional empaty in AN.

Using cluster analysis emerged two groups form both AN and HCs, characterized by good and low Interoceptive ability. Within AN group, the Low perfectionism subgroup showed a significantly higher level of Drive for Thinness, Depressive symptoms and state anxiety, no significant differences were found in BMI, this data showed that Interoception could be linked with more severe Psychopathology but not with malnutrition. In the same direction, in HCs, the subgroup with low Interoception showed a significantly higher level of Bulimia, Body dissatisfaction, depressive symptoms and anxiety and no significant differences in BMI or age. The association between low interoception ability and high level of body dissatisfaction in HCs may be interpretated as a worse relationship with the own body due to the lower ability in listen to and comprehend body signals. Data found are in line with the a -priori hypothesis and confirm previous literature (Pollatos et al., 2008; 2009; Brown et al., 2017; Eshevevari et al., 2014), about the association between Interoception and Anorexia Nervosa Psychopatology and are consisted with the theorized role of interoceptive deficits in maintaining ED symptomathology (Fassino et al., 2004; Pollatos et al., 2009).

Moreover, our data showed that in both AN and HCs, the subgroups with low interoception had significantly lower level of Emotional Competences. Previous literature found correlations between Interoceptive awareness and Alexitymia in AN (Pollatos et al 2008), Eshekevary et al., 2014 found significant correlations between Interoceptive Awareness and Emotional dysregulation in both AN and HCs. The independence of IAc and IA and instead the relationship between IA and emotional susceptibility is confirmed also in healthy women (Calì et al., 2015). These data are in in accordance with the somatic marker hypothesis proposed by Damasio (2004; 2009) and the importance to consider the phenomenology of experience of their own body sensations and the understanding of emotional meanings of the interoceptive sensations in the treatment of AN (Arciero, 2018). From a phenomenological point of view, the core ED psychopathological feature of shape and weight concerns is the result of a disturbance in the way persons with EDs experience their own body and determine their personal identity (Stanghellini et al., 2012). Our data say that AN individuals perceive correctly their own body sensations but probably they do not attribute to them the correct meanings in term of emotions but also in term of hungry and satiety, it may be derived from the attitude to repress emotional expression learned from infancy, frequently clinically observed.

Moreover, running regression analysis, data showed significantly association between both Interoceptive Awareness and emotional competences and AN psychopatology after controlling for age and years of education that were not matched between AN and HCs.

AN patient seems to correctly perceive body signals, but they cannot manage and interpret them correctly, these contribute to deficit in emotional recognition and regulation reported in literature and is associated with eating disorders psychopathology. The failure in managing correctly body signals could lead individuals to find an alternative to perceive themselves, not from their own body but from the others or from the symptoms that could be considered an instrument to feel in control and manage emotional states in interpersonal relationship (Fassino et al., 2004). These data could support the theory that EDs patients tend to feel oneself from starvation and through the gaze of others (Stanghellini et al., 2012), these tendences correlates with EDs psychopathology, in particular with IA and mediate the relationship between insecure attachment and IA in EDs patients (Monteleone et al., 2017). The interpersonal utilization subscale of PEC that resulted preserved in AN might be interpretated also as a signal that AN patients are externally oriented to others in determine their own identity.

Data presented are interesting to better clarify the role of IA in emotional regulation deficits and AN psychopathology, nevertheless the study have some limitations: a) A larger sample would be preferable and AN patients and HCs were not matched with respect to years of education and age; b) Heart-beat Counting method is a wide used measure for IAc but probably not the best one, in particular for AN patients, could be useful use a measure of IAc linked to others body signals like hungry or satiety; c) The association between IA, Emotional Competences and AN psychopathology should be better investigated, considering also confounding variables like depression or anxiety that are characteristics of eating psychopathology and could influence also IA and emotional competences (Pollatos et al., 2009).

Finally, looking to clinical implications, a key aspect of the treatment of AN is weight restoration (APA,2010; NICE, 2017), food aversion represent a hallmark of this disorder and one of the main obstacle to the treatment (Fassino & Abbate Daga 2013). AN patient reported higher scores on anxiety, hunger, and confusion about internal state in comparison to HCs before and after tasting experiment (Marzola et al., 2020). It should be important consider that patients seem not to be able to attribute adequate sense and meanings to internal state and that this aspect contribute to treatment resistance typical of AN.

4. Conclusions

In closing, the four years PhD research project focused on contribute to analyze psychopathological mechanism of onset and maintenance in patients affected by AN. The studies aimed to deeper examine both cold and hot cognition aspects in AN trying to contribute to that research line that would individuate endophenotypes and biological markers of AN (Talbot et al., 2015; Hatch et al., 2010) to bridges the gap between brain disfunctions and symptoms presentation (Klabunde et al., 2013).

The first study (Buzzichelli et al., 2018) investigated cognitive flexibility and perfectionism in AN (Buzzichelli et al., 2018). Our findings support heightened cognitive inflexibility in individuals with AN, particularly in those with high perfectionism. Perfectionism resulted to be a mediator of the relationship between a measure of set-shifting and drive for thinness in AN. Taken together, these data suggest a complex and non-exclusive association between set-shifting, eating psychopathology and perfectionism. This study confirmed previous literature about cognitive inflexibility in AN and, to our knowledge, for the first time highlight the relationship between cognitive rigidity and perfectionism. Literature is consistent in identify perfectionism as a personality characteristic of AN patients (Coulbert et al., 2015; Anderluh et al., 2003) but the interaction between perfectionism and cognitive rigidity and their relationship with AN psychopathology could be hypothesis from clinical practice, is confirmed by these data but still need to broader investigation, with a larger sample and a multidimensional scale of perfectionism.

The second study focused on Interoception in AN and its relationship with emotional competences and AN psychopatology (Buzzichelli et al., in preparation). In accordance with the ‘‘somatic marker’’ hypothesis of Damasio (1994, 1999) stating that the meta-representation of bodily states constitutes an emotional feeling, accessible to consciousness, the a-priori hypothesis was to find deficit in IAc and IA in AN and an association between Interoception ability and emotional competences in both AN and HCs.

Our data highlight, partially in contrast with a-priori hypothesis, deficit in IA but not in IAc, patients affected by AN seems to correctly perceive body signals, but they can’t manage and interpret them correctly. Moreover, data showed significant decreased emotional competences in AN in comparison with HCs and confirm the a-priori hypothesis finding a positive association between IA and emotional competences both in AN than in HCs, low interoceptive awareness is associate to poor emotional competences. With the best of our knowledge, till now, no data were available on the association between Interoceptive ability and emotional competences in AN. Moreover, deficit in both IA and emotional competences resulted associated with anorexia nervosa psychopathology, this data confirms previous literature that identify poor Interoception and

emotional competences as characteristics of AN patients (Pollatos et al., 2008; Abbate -daga et al., 2015).

Data emerged are interesting and open new awareness on which are the psychological point underpinned to symptoms, nevertheless had several limitations, other studies are needed to replicate these findings. Nevertheless, the role of cognitive rigidity, perfectionism, IA and emotional competences in AN should be taken into account in developing tailored treatment and in everyday clinical activity to manage with treatment resistance typical of AN patients.

Looking at therapeutic approaches, the CRT (Cognitive Remediation Therapy; Tchanturia et al., 2017) has been developed with the specific aim to target cognitive rigidity in patients with AN. Through increasing flexibility in thinking and making small, manageable changes, CRT has the potential to increase the success of other psychological therapies for AN (Pretorius & Tchanturia, 2007). Others study found a significant improvement in cognitive profile after CRT sessions (Abbate-Daga et al., 2012; Tchanturia et al., 2008) but also in impulse regulation and interoceptive awareness (Abbate Daga et al., 2012) and seems to be effective also on patients' perfectionism (Pitt et al., 2010). CRT seems to be useful in involving patients in treatment and in motivating them to further psychotherapy. Perfectionism-focused treatment as proposed by Lloyd et al., (2015) could be fundamental in improve awareness of these tendences in AN patients and the way in which these personality aspect could be link with symptoms maintenance and resistance to treatment.

The whole panorama of psychotherapies, with different approaches, consider personal and interpersonal emotional word fundamental, less common is to consider body sensations from which emotions raises. Research about Interoception in AN open to the phenomenological theory (Arciero & Bondolfi, 2009; Arciero et al., 2019) of the needed to come back to the basic first-person experience, including body sensations, to allow individuals to give new emotional sense. It seems clear that individuals with AN have to learn to listen to and trust in their interoceptive signals giving adequate emotional interpretation that could lead to regulate themselves on the basis of their own sensations and emotions and not on starvation or only the gaze of the others (Stanghellini et al., 2012).

Further research would be recommended to improve the therapeutic armamentarium in this regard.

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