

Decision-making functioning as a predictor of treatment outcome in anorexia nervosa

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Abstract

The pathological eating behaviour of patients with anorexia nervosa reflects a deficit in planning real-life strategies that can be observed in an experimental setting through the Gambling Task, a tool designed to detect and measure decision-making abilities. We examined the role of Gambling Task performance as a predictor of treatment outcome in anorectic patients, and we evaluated changes in decision-making after clinical improvement. Performance on the Gambling Task was evaluated, and a clinical–nutritional assessment of 38 anorectic patients was carried out before and after a cognitive–behavioural and drug treatment program. Task performance of anorectic patients was compared with that of 30 healthy control participants. Patients who had a better decision-making profile at baseline showed significantly greater improvement in nutritional status. The decision-making deficiency of some anorectic patients is probably linked to those individual features that contribute to the phenomenological expression of the disorder and to its different treatment outcomes.

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1. Introduction

The pathological eating behaviour of patients with anorexia nervosa (AN) reflects an impairment in planning real-life strategies. This deficit could account for the inability of some AN patients to take a long-term perspective and their preference to opt for choices that yield high immediate gains in spite of higher future losses (Cavedini et al., 2004a). The preference of AN patients for choices that are advantageous in the short-term but not in the long run is

confirmed from their impaired performance on tasks modelling real-life decision-making processes. For example, during the acute phase of illness, AN patients are impaired on the Gambling Task (GT) (Cavedini et al., 2004a), a measure of decision-making propensities (Bechara et al., 1994). Their poor performance on this neuropsychological test does not appear to be related to illness severity, thus suggesting the absence of any relationship between nutritional status, severity of symptoms and general cognitive impairment in these patients (Lauer et al., 1999).

Similar decision-making impairments, detected in real life as well as in the laboratory with the GT, can also be found in patients with obsessive–compulsive disorder (Cavedini et al., 2002; Cavallaro et al., 2003),

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to the extent that several authors suggested that AN could be considered as a form of obsessive–compulsive disorder (Halmi et al., 2003). Indeed, evidence from clinical, family and genetic studies suggests the inclusion of AN within the obsessive–compulsive spectrum (Matsunaga et al., 1999; Cavallini et al., 2000; Bellodi et al., 2001).

However, the decision-making profile of patients with obsessive–compulsive disorder, as reflected by their performance on the GT, shows important individual differences. A further investigation observed that those subjects who perform poorly on the GT go on to show a poor clinical outcome to pharmacological anti-obsessive treatment with serotonin re-uptake inhibitors (Cavellini et al., 2002), indicating the GT may be a predictor of clinical outcome and suggesting the identification of obsessive–compulsive patients with specific traits significantly associated to clinical outcome (Erzegovesi et al., 2001; Alonso et al., 2001). It would be valuable if similar cognitive deficits in AN patients could be used to predict clinical outcome and aid in the development of optimal treatment strategies (Fassino et al., 2001).

The present study is a continuation of our studies on decisional processes in obsessive–compulsive spectrum disorders and stems from our previous study on AN (Cavellini et al., 2004a). A subgroup of the patients in the current study ($n=12$, 28.5%) were also included in the earlier report.

2. Methods

2.1. Sample

Forty-two female participants with AN among those referred to the Eating Disorders Clinical and Research In-patients Unit of San Raffaele Scientific Institute of Milan agreed to participate to the study, over a period of 10 months. Thirty-eight participants (18 with AN restricting subtype, AN-r, and 20 with AN binge-eating/purge subtype, AN-be) were included in the study while four dropouts were excluded (see Section 2.3).

Exclusion criteria for AN patients were lifetime psychiatric disorders other than anorexia, major medical diseases, neurological syndromes, brain injury or trauma, drug or alcohol abuse, use of any psychotropic drugs in the previous 6 weeks and receiving any other kind of therapy (i.e. behavioural therapy). Consensus diagnoses, according to DSM-IV criteria (American Psychiatric Association, 1994), were obtained by two senior psychiatrists who independently assessed all

participants using a clinical interview and the MINI International Neuropsychiatric Interview-Plus (Sheehan et al., 1998), a diagnostic interview designed to meet the need for a short but accurate structured psychiatric interview for DSM-IV and ICD-10 disorders. The severity of eating symptoms was assessed with the Yale–Brown Cornell Eating Disorder Scale (YBC–EDS) (Mazure et al., 1994) while the physical condition of the patients was examined with the Body Mass Index (BMI) expressed as kg/m^2 .

Thirty female healthy controls (HC), matched for age and education to the AN participants, recruited through local advertisements among college students, administrative and workers' staff of the hospital, agreed to participate in the study. The control participants were free of any lifetime psychiatric disorder, medical or neurological diseases and drug or alcohol abuse. All the participants gave their written informed consent to participate after the procedure and possible side effects had been fully explained.

2.2. Assessment

Patients and control participants were assessed with the following neuropsychological tasks: (a) the Gambling Task (GT) specific for the investigation of decision-making, (b) Weigl's Sorting Test and (c) the Object Alternation Test for the assessment of two other cognitive functions different from decision-making, in order to investigate whether patients were impaired just in decision-making or in general cognitive domains. These neuropsychological tasks were administered by a trained neuropsychologist in a single session and in a randomized sequence; the complete testing session never required more than 90 min, and all participants completed the tests without any problems in cooperation or fatigue.

2.2.1. Gambling Task (Bechara et al., 1994)

The subject is given a loan of play money, and the task requires making 100 card selections from four decks. The output of each selected card can be either a gain or a gain and a loss of money: decks A and B are “disadvantageous” in the long run because the total gain is lower than the total loss, while decks C and D are “advantageous” because the penalties are lower. The goal of the task is to maximize profit. The score reported is based on the difference between the number of “advantageous” minus the number of “disadvantageous” cards selected (net score).

The task was also administered after the treatment program (see Section 2.3): for this purpose, the output

of the different decks, concerning the magnitude and the frequency of punishment, has been changed (A→B; B→D; C→A; D→C) to reduce the risk of a learning effect.

2.2.2. Weigl's Sorting Test (Weigl, 1941)

This tool assesses the subject's ability to shift from one strategy to another. The scores, which range from 0 to 5, are on the number of categories that the subject recognizes.

2.2.3. Object Alternation Test (Freedman, 1990)

This tool assesses the subject's ability to find a strategy according to the use of feedback. The performance was calculated as the total number of perseverative errors.

2.3. Study design and treatment protocol

Patients' assessments were performed at admission to and at discharge from the in-patient Unit for Eating Disorder. At admission, the MINI International Neuropsychiatric Interview-Plus was administered to all candidates for the study: to the suitable subject, who decided to participate in the study, the neuropsychological battery and the YBC-EDS were administered and the BMI score was calculated. Then, patients started treatment according to a cognitive-behavioural program based on a lenient operant conditioning approach (Bhanji and Thomson, 1974; Garner and Bemis, 1982) (details provided on request). Patients were also assigned to a standardized treatment schedule according to a 1:3 single-blind design with flexible doses: fluvoxamine (150–300 mg/day, $n=14$), fluoxetine (20–60 mg/day, $n=14$), and placebo ($n=14$), so that one subgroup of patients ($n=28$) also received treatment with selective serotonin reuptake inhibitor (SSRI) drugs (cognitive-behavioural treatment program plus SSRIs, AN-cbt/d) while the other subgroup ($n=14$) were treated only with a cognitive-behavioural program (cognitive-behavioural treatment program plus placebo, AN-cbt/p). Three AN patients from the fluvoxamine group and one AN patient from the fluoxetine group dropped out at the beginning of the study because of lack of compliance or severe side effects; the dropouts were not included in the data analysis.

At discharge, the YBC-EDS was administered and the BMI score was calculated. The GT was re-administered to evaluate possible modifications in the decision-making strategy with the improvement of psychopathological and physical conditions.

The healthy control participants were assessed with the MINI International Neuropsychiatric Interview and the neuropsychological battery at baseline (T_0); the GT was re-administered 6 weeks from T_0 , to evaluate a possible learning effect on this task.

2.4. Statistical procedure

Data were collected in a personal computer and analysed with the Statistical Package for Windows. Data from the GT performance were examined by comparing the differences between the total number of advantageous cards (C and D decks) minus the total number of disadvantageous cards (A and B decks) selected.

Moreover, the mean scores on the GT were transformed into an index of good (GT+) or bad (GT-) performance for each patient. To obtain this qualitative index, we applied receiver operator characteristic analysis (ROC) (Metz and Kronman, 1987) to the GT performance of a larger independent sample of anorectic patients ($n=100$) and healthy control subjects ($n=120$), which identified a cutoff of ≥ 51 cards selected from decks A and B as the index of bad performance (critical test value for the corresponding operating point on the fitted binomial ROC curve: TPF=0.783, FPF=0.753; binomial ROC parameters: $A=-0.673$, $B=1.033$, correlation=-0.362) (Cavedini et al., 2004b). This cutoff was applied to the GT performances of the patients in this study. Consistency and reliability on this task between the two AN cohorts were assessed (details provided upon request).

2.4.1. χ^2 test, t-test for independent samples and one-way analysis of variance (ANOVA)

These tests were used to compare: (a) demographic and clinical characteristics between HC vs. AN, AN-r vs. AN-be, AN-cbt/p vs. AN-cbt/d, among AN patients with good or bad GT performance; and (b) differences between admission and discharge in YBC-EDS and BMI scores and GT performance.

2.4.2. One-way and two-way analysis of variance (ANOVA) with repeated measures

This approach was used to examine: (a) intergroup (AN vs. HC, AN-r vs. AN-be, AN-cbt/p vs. AN-cbt/d) differences in GT performance at admission, and between admission and discharge; (b) the relationship between treatment outcome and GT performance in AN, AN-r and AN-be; (c) differences between admission and discharge in YBC-EDS and BMI scores, according to GT performance, in AN, AN-r and AN-

be; (d) the relationship between treatment outcome and kind of treatment in AN; and (e) other neuropsychological measures among AN vs. HC, AN-r vs. AN-be.

2.4.3. Standard multiple regression analysis

Multiple regression analysis was used in AN to correlate GT at admission to YBC-EDS and BMI scores. A casewise multiple regression analysis was performed using Δ BMI (discharge minus admission BMI scores) as the dependent variable and duration of hospitalization as the independent variable.

3. Results

3.1. Clinical and demographic characteristics

Clinical and epidemiological characteristics of the AN and HC groups were compared, and no differences were found for age (HC: mean=22.6, S.D.=4.1 years; AN: mean=24.5, S.D.=5.2 years; $P=0.1$) or education (HC: mean=12.4, S.D.=2.9 years; AN: mean=13.1, S.D.=3.2 years; $P=0.3$). Mean scores for clinical and physical characteristics of the AN sample on admission were 5.2 years (S.D.=3.5) for duration of illness, 26.4 (S.D.=7.1) for YBC-EDS total score, 14.1 (S.D.=2.8) for YBC-EDS score for preoccupations, 12.3 (S.D.=4.9) for YBC-EDS score for rituals, and 14.2 (S.D.=1.7) for BMI. The mean length of hospitalization for AN patients was 127.6 (S.D.=44.1) days.

The only differences that we found regarded demographic and clinical characteristics of the AN sample according to clinical subtypes (restricting subtype,

AN-r, $n=18$ vs. binge-eating/purge subtype, AN-be, $n=20$) (Table 1) and treatment program groups (cognitive-behavioural treatment program plus placebo, AN-cbt/p, $n=14$ vs. cognitive-behavioural treatment program plus SSRIs, AN-cbt/d, $n=24$) (Table 2). The AN-r and AN-be subgroups differed in duration of illness ($t=-3.56$, $df=1,36$, $P=0.0001$), BMI at admission ($t=-3.98$, $df=1,36$, $P=0.0001$) and BMI at discharge ($t=-3.15$, $df=1,36$, $P=0.005$). These differences are expected since the binge-eating subtype of AN is in general characterized by a longer period of illness and a higher BMI. No significant differences were found between the AN cbt/p and AN cbt/d subgroups for all the variables we considered.

3.2. Decision-making performances at admission

Table 3 summarizes GT performances of the HC and AN groups at admission. As expected, a one-way ANOVA performed between HC and AN, using the net score on the GT as the dependent variable, was significant ($F=15.54$, $df=1,66$, $P=0.0001$), showing a difference in decision-making profile between HC and AN. The poor performance of the AN group did not appear to be related to severity of illness as shown by the absence of any significant correlation of the GT score with the YBC-EDS total score ($F=2.03$, $R^2=0.03$, $P=0.1$) or the BMI score ($F=1.71$, $R^2=0.02$, $P=0.4$).

Moreover, among the AN patients, both the AN-r and AN-be subgroups preferred disadvantageous decks; in fact, a one-way ANOVA performed between the two groups, using the net score on the GT as the

Table 1
Differences in demographic and clinical characteristics in patients with anorexia nervosa according to clinical subtype

Variables		AN-r [$n=18$; mean (S.D.)]	AN-be [$n=20$; mean (S.D.)]	<i>P</i> -level
Demographics characteristics	Age	23.8 (4.4)	21.5 (3.5)	0.08
	Education (years)	12.4 (2.3)	12.5 (3.6)	0.9
Characteristics of illness	Age at onset	18.2 (3.4)	16.8 (3.1)	0.2
	Duration of illness (years)	3.3 (2.6)	6.9 (3.5)	0.0001 ^a
Clinical values at admission	YBC-EDS total score	25.4 (5.3)	27.5 (8.7)	0.4
	YBC-EDS score for preoccupations	13.3 (2.6)	14.8 (2.8)	0.09
	YBC-EDS score for rituals	11.9 (3.3)	12.7 (6.2)	0.6
	BMI score	13.2 (1.3)	15.1 (1.6)	0.0001 ^b
Clinical values at discharge	YBC-EDS total score	9.2 (7.5)	10.6 (7.7)	0.6
	YBC-EDS score for preoccupations	5.1 (3.9)	6.3 (3.7)	0.3
	YBC-EDS score for rituals	4.1 (3.8)	4.4 (4.2)	0.8
	BMI score	14.9 (1.8)	16.8 (1.9)	0.005 ^c
Hospitalisation	Duration (days)	139.9 (36.9)	117.7 (48.1)	0.1

AN-r=anorexia, restricting subtype; AN-be=anorexia, binge-eating/purge subtype.

^a $t=-3.56$, $df=1,36$.

^b $t=-3.98$, $df=1,36$.

^c $t=-3.15$, $df=1,36$.

Table 2
Differences in demographic and clinical characteristics in patients with anorexia nervosa according to treatment subtype

Variables		AN-cbt/p [<i>n</i> = 14; mean (S.D.)]	AN-cbt/d [<i>n</i> = 24; mean (S.D.)]	<i>P</i> -level
Demographics characteristics	Age	23.1 (4.2)	22.6 (4.1)	0.7
	Education (years)	12.6 (2.9)	12.3 (3.1)	0.8
Characteristics of illness	Age at onset	17.9 (3.3)	17.9 (3.2)	0.1
	Duration of illness (years)	5.2 (3.7)	5.1 (3.3)	0.9
Clinical values at admission	YBC–EDS total score	26.4 (8.3)	26.6 (4.7)	0.9
	YBC–EDS score for preoccupations	14 (2.9)	14.1 (2.5)	0.9
	YBC–EDS score for rituals	12.3 (5.7)	12.3 (3.1)	0.9
	BMI score	14.2 (1.7)	14.2 (1.9)	0.9
Clinical values at discharge	YBC–EDS total score	11.1 (8)	7.8 (5.9)	0.1
	YBC–EDS score for preoccupations	6.2 (4.1)	4.8 (2.8)	0.2
	YBC–EDS score for rituals	4.8 (4.1)	3 (3.4)	0.1
	BMI score	15.8 (2.1)	16 (2)	0.7
Hospitalisation	Duration (days)	118.7 (46)	147.1 (33.9)	0.5

AN-cbt/p=anorexia, cognitive-behavioral treatment program *plus* placebo; AN-cbt/d=anorexia, cognitive-behavioral treatment program *plus* SSRIs.

dependent variable, was not significant ($P=0.1$). Finally, according to treatment subtypes, a one-way ANOVA performed between groups (AN-cbt/p vs. AN-cbt/d), using the net score on the GT as the dependent variable, was not significant ($P=0.5$).

3.3. Decision-making performances at discharge

Table 3 presents the GT performances of the HC group and the AN group at discharge. To exclude a possible learning effect in the retest procedure of the GT, we readministered the task to the HC group 6 weeks from the first administration, and we failed to find any significant difference in performance ($P=0.3$). Afterwards, we evaluated possible modifications in the decision-making functioning of AN patients after amelioration of their symptoms and weight gain. No differences were found when patients were retested: in fact, a one-way ANOVA performed among the two groups (GT at admission vs. GT at discharge), using the net score on the GT as the dependent variable, was not significant ($P=0.7$). The same analysis performed according to AN subtype was not significant for either

the AN-r subtype ($P=0.5$) or the AN-be subtype ($P=0.7$).

3.4. Quantitative to qualitative analysis of the GT

After a quantitative analysis of the GT, the qualitative profile of decision-making was also evaluated applying a cutoff point of good versus bad performance to our study sample (see Section 2.4 for details). The percentage of good performance (GT+) among the HC group was 76.6% ($n=23$) compared with 34.2% in the AN group ($n=13$) ($\chi^2=10.48$, $df=1$, $P=0.001$). Although the difference was not significant ($P=0.2$), there were more GT good performers among AN-be (45%) than the AN-r (22.3%) patients.

To evaluate whether performance on the GT was related to illness characteristics, ANOVAs were performed using the GT profile (GT+ or GT-) as the grouping factor and clinical or epidemiological characteristics at admission as the dependent variables: no differences were found between the two groups for YBC–EDS total score ($P=0.8$), YBC–EDS score for preoccupations ($P=0.8$) and rituals ($P=0.6$), BMI

Table 3

Mean number of cards selected from advantageous *minus* disadvantageous decks at the Gambling Task: differences between admission and discharge performances in controls subjects and anorectic patients

Subjects	Admission [mean (S.D.)]	Discharge [mean (S.D.)]	<i>P</i> -level
AN sample ($n=38$)	-4.89 (17.1)	-3.78 (14.3)	0.7
AN-r ($n=18$)	-9.22 (20.1)	-5.27 (11.6)	0.5
AN-be ($n=20$)	-1 (13.1)	-2.45 (16.4)	0.7
AN-cbt/p ($n=14$)	-2 (15.3)	-1.4 (11.9)	0.9
AN-cbt/d ($n=24$)	-5.75 (17.7)	-5.2 (15.2)	0.9
HC ($n=30$)	8.5 (8.2)	13 (10.3)	0.3

AN-r=anorexia, restricting subtype; AN-be=anorexia, binge-eating/purge subtype; AN-cbt/p=anorexia, cognitive-behavioral treatment program *plus* placebo; AN-cbt/d=anorexia, cognitive-behavioral treatment program *plus* SSRIs; HC=healthy controls.

score ($P=0.8$), other cognitive tests (Object Alternation Test, $P=0.7$; Weigl Sorting Test, $P=0.9$) and epidemiological variables (age, $P=0.7$; education level, $P=0.5$; age at onset, $P=0.9$; duration of illness, $P=0.1$).

Chi-square analyses were performed to evaluate changes in GT performance between admission and discharge. In the AN patients, 65.8% ($n=25$) at admission and 55.2% ($n=21$) at discharge performed the GT using a suboptimal strategy ($P=0.3$). In detail, we found 52.7% ($n=20$) of patients performed badly on the GT both at admission and discharge, whereas 31.6% ($n=12$) of patients performed well on the GT both at admission and discharge; as for the rest of the patients, considering the ones with a different performance from admission to discharge, 13.1% ($n=5$) of them shifted their performance from bad to good, while 2.6% ($n=1$) of them shifted their performance from good to bad ($\chi^2=15.28$, $df=1$, $P=0.001$).

3.5. Performance on the GT and treatment outcome

Comparisons between admission and discharge show that after treatment, the AN-r and AN-be subgroups improved significantly in the YBC-EDS total score (AN-r, $t=7.48$, $df=1,34$, $P=0.0001$; AN-be, $t=6.50$, $df=1,38$, $P=0.0001$), subtotal scores for pre-occupations and for rituals, and in BMI (AN-r, $t=-3.24$, $df=1,34$, $P=0.003$; AN-be, $t=-3.06$, $df=1,38$, $P=0.004$) (Table 1). Similarly, improvement was found for the AN-cbt/p and AN-cbt/d subgroups in the YBC-EDS total score (AN-cbt/p, $t=4.90$, $df=1,26$, $P=0.0001$; AN-cbt/d, $t=12.2$, $df=1,46$, $P=0.0001$), subtotal scores for pre-occupations and for rituals, and in BMI score (AN-cbt/p, $t=-2.42$, $df=1,26$, $P=0.02$; AN-cbt/d, $t=-3.19$, $df=1,46$, $P=0.003$) (Table 2).

Afterwards, we studied the value of the GT as a predictor of treatment outcome of AN patients, using changes in BMI and YBC-EDS score between admission and discharge as the indices of improvement. A two-way ANOVA with repeated measures, using good or bad GT performance (GT group) as the independent variable and BMI at admission and discharge (Time) as dependent variables, showed a significant Time \times GT group interaction ($F=11.13$, $P=0.002$). We then performed the same analyses in the AN-r and AN-be subgroups. A significant Time \times GT group interaction was found for the AN-be subgroup ($F=11.12$, $P=0.004$) but not for the AN-r subgroup ($P=0.09$) (Fig. 1). No significant differences were found when the YBC-EDS total score ($P=0.1$) and subtotal scores

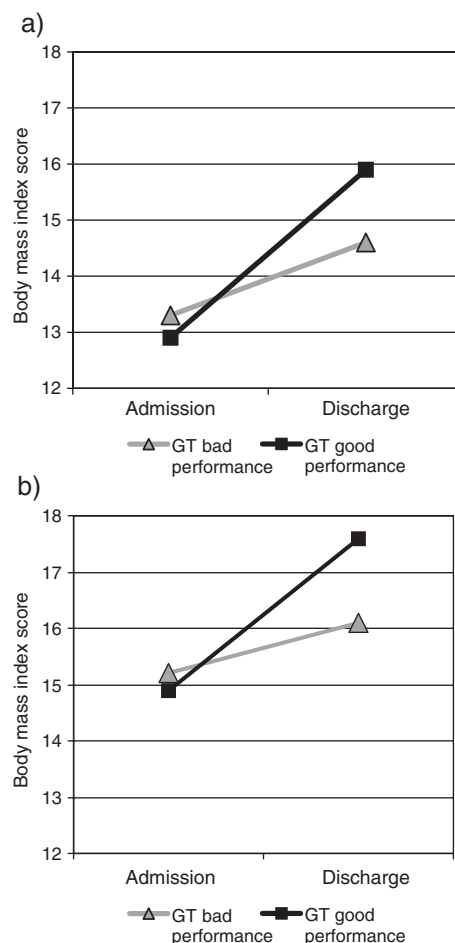


Fig. 1. The predictive role of the Gambling Task in treatment outcome: increase in body mass index after treatment according to bad or good performance on the task in the restricting subtype (a) and the binge-eating/purge subtype (b).

for pre-occupations ($P=0.1$) and rituals ($P=0.2$) were entered as the dependent variables.

To exclude the influence of different kinds of treatments or of the duration of hospitalization on the predictive value of the GT in BMI changes, we performed other analyses. A two-way ANOVA with repeated measures, which used good or bad GT performance (GT group) and type of treatment (Treatment) as independent variables and the BMI at admission and discharge (Time) as dependent variables, showed a significant Time \times GT group interaction ($F=9.63$, $P=0.004$) but not a significant Time \times Treatment interaction ($P=0.7$).

Nevertheless, a casewise multiple regression analysis was performed using Δ BMI (BMI at discharge minus BMI at admission) as the dependent variable and duration of hospitalization as the independent variable. We excluded any significant effect of hospitalization on BMI changes ($F=3.39$, $P=0.08$, $R^2=0.06$).

3.6. Other neuropsychological tests

In comparisons of the performance of the HC and AN subjects on the other neuropsychological tests, no differences ($P=0.9$) were found in the number of categories recognized on Weigl's Sorting Test (HC: mean=4.4, S.D.=0.9; AN: mean=4.3, S.D.=0.7) or for the total number of perseverative errors on the Object Alternation Test (HC: mean=3.4, S.D.=2.6; AN: mean=2.7, S.D.=2; $P=0.05$). The AN subgroups also showed no significant differences in their performances on the two tests (Weigl's Sorting Test, AN-r: mean=4.2, S.D.=0.6; AN-be: mean=4.4, S.D.=4.2; Object Alternation Test, AN-r: mean=2.7, S.D.=1.8; AN-be: mean=2.6, S.D.=1.9).

4. Discussion

Anorexia nervosa is a psychiatric illness characterized by the fear of gaining weight and by a consequent behaviour involving a progressive reduction and/or rejection of food. When hungry, anorectic patients choose to progressively avoid introducing calories in order to obtain an immediate reward, i.e. the relief of anxiety elicited by food phobia, ignoring the long-term negative consequences of their choices, i.e. the progressive and severe decline of their physical condition. Altogether, they seem unable to correctly orient their eating behaviour.

The pathological eating actions of these patients could be the expression of their inability to modulate reward and punishment in a long-term perspective, thus leading to a deficit in planning real-life strategy. Testing decision-making with the GT, we attempted to find a neuropsychological measure related to the cognitive and behavioural pattern of anorectic psychopathology. In fact, there are some remarkable similarities between the GT performance of these patients and their real life pathological behaviours.

In this study, we confirmed the presence of a decision-making impairment in AN patients, as previously found in a larger sample (Cavadini et al., 2004a). In fact, on the GT, the patients opt for choices that yield high immediate gains in spite of higher future losses, with differences in the severity of this impairment between restricting and binge-eating/purge subtypes.

This deficit is unlikely to be a non-specific malfunctioning due to starvation, as shown by the absence of any correlation between task performance and severity of illness or BMI score. Nevertheless, differences in epidemiological and clinical characteristics between restricting and binge purge/eating subtypes seem not

to influence decision-making differences between the two groups.

Besides, heterogeneity in GT performance was found in these patients. In fact, a qualitative analysis of the GT performance revealed that some patients (34.2%) performed the task as well as control subjects. This heterogeneity of performance does not appear to depend on nutritional status, severity of illness or general cognitive functioning.

Nevertheless, the greater prevalence of bad performance at the GT found among the restricting subtype (77.7%) but not among the binge purge/eating subtypes (55%), even if not significant, could be interpreted as evidence of a greater severity of the restricting subtype. Perhaps, this decision-making heterogeneity could be explained by the different strategies that these patients use to make up for their fear of gaining weight, which leads to a restricting or a binge-eating/purge behaviour.

The decision-making impairment seems to be stable over time and not to depend on physical and clinical modifications after treatment. In fact, when evaluated at discharge after clinical and physical amelioration, performance of AN patients was similar to their performance at the time of admission. This finding suggests that decision-making is probably independent of the primary etiopathogenetic mechanisms of AN and is linked to those individual features that contribute to the phenomenological expression of the disorder (restricting vs. binge-eating) and to its different treatment outcomes.

The retesting session used the same task in which the position of the decks was changed in order to counter learning effects. This strategy seems to have been successful since we did not find a learning effect in either the control subjects or the patients. This may not be significant because the variance may be too high and it may become significant with a larger sample, but the main point is that our patients do not show any kind of improvement at the retest. These data can be compared with the earlier reports that show that patients do not improve their GT performance at the retest (Bechara et al., 2000) and are in accord with the observation that in AN patients dysfunctional decision-making is a trait condition instead of a state condition.

Another important observation is that the impaired performance on the GT could not be explained as a non-specific reflection of negative effects of starvation or sickness. Otherwise performance on the other two cognitive tests (Weigl's Sorting Test and Object Alternation Test) should also have been impaired, but this was not the case.

With regard to treatment outcome, it may be suggested that anorectic patients with normal decision-making ability succeed in taking advantage from a treatment program based on the operant conditioning paradigm during cognitive–behavioural therapy, as shown by a significant gain in BMI score after treatment. On the contrary, the inability to identify an adequate decision-making strategy prevents anorectic patients with bad performances on the GT from taking significant advantage of the same program.

A preserved decision-making ability in patients with obsessive–compulsive disorder probably reflects a sensitivity of circuits involved in this disorder to serotonin re-uptake inhibitors. In fact, the GT performance in obsessive–compulsive disorder discriminated between subjects responsive to anti-obsessive pharmacological treatments with serotonin re-uptake inhibitors and those who are non-responders, for whom the use of an augmentation strategy with atypical antipsychotic drugs increases the benefit of the anti-obsessive treatment (McDougle et al., 2000). These findings support the large number of considerations suggesting that a decision-making deficit may reflect an altered neuromodulation of the orbitofrontal cortex and the interconnected limbic–striatal system by both the ascending serotonin and mesocortical dopamine projections (Rogers et al., 1999).

With regard to AN, no differences were found in outcome measures between patients treated with or without pharmacological therapy during the hospitalisation. Even if this seems to exclude the efficacy of drug therapy with serotonin re-uptake inhibitors (Ferguson et al., 1999) in the acute phase of anorexia, our treatment plan did not allow us to evaluate any differential contribution of pharmacological and cognitive–behavioural therapy components in the treatment of these patients or a ceiling effect of cognitive–behavioural therapy that could mask any drug effect when present in terms of efficacy. In this case, the ability to gain advantage from the cognitive–behavioural therapy, linked to the efficiency of the decision-making function, could not be further enhanced by pharmacological treatment with serotonin re-uptake inhibitors, while an alternative pharmacological strategy, such as adding atypical antipsychotics to serotonin re-uptake inhibitors, as binge-eating has been done for unresponsive obsessive–compulsive disorder patients (McDougle et al., 2000), should give better results.

Some limitations should be kept in mind reading these results. First of all, a larger sample size would have been desirable and further effort should be made in the future to obtain a more homogeneous sample, more

numerous subgroups and to improve the lack of homogeneity on some variables, particularly concerning differences between restricting and binge-eating/purge subtypes. Moreover, caution should be taken regarding the definition of anorexia nervosa subtypes since some lines of research suggest that the restricting subtype represents a phase in the course of anorexia rather than a distinct subtype. Finally, different decision-making tasks should be administered to better understand decisional processes and to clarify how these processes work, in order to assess how an individual patient's pattern of choices might alter across a range of well-defined and clearly presented contingencies, instead of the condition in which the underlying contingencies relating actions to relevant outcomes remain hidden. These considerations should be relevant to improve the behavioural treatment strategy in anorexia nervosa.

Further studies are needed to better understand the role of neural functions related to decision-making as a predictor of treatment outcome in anorexia nervosa and to investigate how it could be a criterion for choosing the proper treatment. Also in obsessive-compulsive disorder, decision-making should be already considered as an effective criterion for pharmacological treatment choice given that antiobsessive treatment outcome is increased by choosing an appropriate drug strategy according to the decision-making performance (Cavedini et al., 2004b). Nevertheless, this study provides further evidence about the existence of a common clinical and biological spectrum to which anorexia nervosa and obsessive–compulsive disorder belong.

References

- Alonso, P., Menchon, J.M., Pifarre, J., Mataix-Cols, D., Torres, L., Salgado, P., Vallejo, J., 2001. Long-term follow-up and predictors of clinical outcome in obsessive–compulsive patients treated with serotonin reuptake inhibitors and behavioral therapy. *Journal of Clinical Psychiatry* 62, 535–540.
- American Psychiatric Association, 1994. *Diagnostic and Statistical Manual of Mental Disorders*, Fourth edition. APA, Washington, DC.
- Bechara, A., Damasio, A.R., Damasio, H., Anderson, S.W., 1994. Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition* 50, 7–15.
- Bechara, A., Tranel, D., Damasio, H., 2000. Characterization of the decision-making deficit in patients with ventromedial prefrontal cortex lesions. *Brain* 123, 2189–2202.
- Bellodi, L., Cavallini, M.C., Bertelli, S., Chiapparino, D., Riboldi, C., Smeraldi, E., 2001. Morbidity risk for obsessive–compulsive spectrum disorders in first-degree relatives of patients with eating disorders. *American Journal of Psychiatry* 158, 563–569.
- Bhanji, S., Thomson, J., 1974. Operant conditioning in the treatment of anorexia nervosa: a review and retrospective study of 11 cases. *British Journal of Psychiatry* 124, 166–172.

- Cavallaro, R., Cavedini, P., Mistretta, P., Bassi, T., Angelone, S.M., Ubbiali, A., Bellodi, L., 2003. Basal–cortico-frontal circuits in schizophrenia and obsessive–compulsive disorder: a controlled, double dissociation study. *Biological Psychiatry* 54, 437–443.
- Cavallini, M.C., Bertelli, S., Chiapparino, D., Riboldi, S., Bellodi, L., 2000. Complex segregation analysis of obsessive–compulsive disorder in 141 families of eating disorder probands, with and without obsessive–compulsive disorder. *American Journal of Medical Genetics* 96, 384–391.
- Cavedini, P., Riboldi, G., D’Annunzi, A., Belotti, P., Cisima, M., Bellodi, L., 2002. Decision-making heterogeneity in obsessive–compulsive disorder: ventromedial prefrontal cortex function predicts different treatment outcomes. *Neuropsychologia* 40, 205–211.
- Cavedini, P., Bassi, T., Ubbiali, A., Casolari, A., Giordani, S., Zorzi, C., Bellodi, L., 2004a. Neuropsychological investigation of decision-making in anorexia nervosa. *Psychiatric Research* 127, 259–266.
- Cavedini, P., Bassi, T., Zorzi, C., Bellodi, L., 2004b. The advantages of choosing antiobsessive therapy according to decision-making functioning. *Journal of Clinical Psychopharmacology* 24, 1–4.
- Erzegovesi, S., Cavallini, M.C., Cavedini, P., Diaferia, G., Locatelli, M., Bellodi, L., 2001. Clinical predictors of drug response in obsessive–compulsive disorder. *Journal of Clinical Psychopharmacology* 21, 488–492.
- Fassino, S., Abbate Daga, G., Amianto, F., Leombruni, P., Garzaro, L., Rovera, G.G., 2001. Nonresponder anorectic patients after 6 months of multimodal treatment: predictors of outcome. *European Psychiatry* 6, 466–473.
- Ferguson, C.P., La Via, M.C., Crossan, P.J., Kaye, W.H., 1999. Are serotonin selective reuptake inhibitors effective in underweight anorexia nervosa? *International Journal of Eating Disorders* 25, 11–17.
- Freedman, M., 1990. Object alternation and orbitofrontal system dysfunction in Alzheimer’s and Parkinson’s disease. *Brain and Cognition* 14, 134–143.
- Garner, D.M., Bemis, K.M., 1982. A cognitive behavioural approach to anorexia nervosa. *Cognitive Therapy and Research* 6, 123–150.
- Halmi, K.A., Sunday, S.R., Klump, K.L., Strober, M., Leckman, J.F., Fichter, M., Kaplan, A., Woodside, B., Treasure, J., Berrettini, W.H., Al Shabbat, M., Bulik, C.M., Kaye, W.H., 2003. Obsessions and compulsions in anorexia nervosa subtypes. *International Journal of Eating Disorders* 33, 308–319.
- Lauer, C.J., Gorzewski, B., Gerlinghoff, M., Backmund, H., Zihl, J., 1999. Neuropsychological assessments before and after treatment in patients with anorexia nervosa and bulimia nervosa. *Journal of Psychiatric Research* 33, 129–138.
- Matsunaga, H., Kiriike, N., Iwasaki, Y., Miyata, A., Yamagami, S., Kaye, W.H., 1999. Clinical characteristics in patients with anorexia nervosa and obsessive–compulsive disorder. *Psychological Medicine* 29, 407–414.
- Mazure, C.M., Halmi, K.A., Sunday, S.R., Romano, S.J., Einhorn, A.M., 1994. The Yale–Brown–Cornell Eating Disorder Scale: development, use, reliability and validity. *Journal of Psychiatric Research* 28, 425–445.
- McDougle, C.J., Epperson, C.N., Pelton, Wasylink, S., Price, L.H., 2000. A double-blind, placebo-controlled study of risperidone addition in serotonin reuptake inhibitor–refractory obsessive–compulsive disorder. *Archives of General Psychiatry* 57, 794–801.
- Metz, C.E., Kronman, H.B., 1987. Statistical significance test for the binomial ROC curves. *Journal of Mathematics in Psychology* 22, 218–243.
- Rogers, R.D., Everitt, B.J., Baldacchino, A., Blackshaw, A.J., Swanson, R., Wynne, K., Baker, N.B., Hunter, J., Carthy, T., Booker, E., London, M., Deakin, J.F., Sahakian, B.J., Robbins, T.W., 1999. Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers. Evidence for monoaminergic mechanism. *Neuropsychopharmacology* 20, 322–339.
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry* 59, 22–33 (Italian version: Conti, L.; Rossi, A.; Donda, P.).
- Weigl, E., 1941. On the psychology of so-called process of abstraction. *Journal of Abnormal and Social Psychology* 36, 3–33.