

Relationship between neuropsychology, clinical traits, psychopathology and attitudes towards change in eating disorders

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Abstract

Background: The interest of research on the neuropsychological characteristics of eating disorders (EDs) has primarily focused on inhibitory control, set-shifting and central coherence, as well as attention bias and decision making. These neuropsychological aspects may also influence attitudes towards therapeutic change and be related to a more severe clinical status.

The objective of this paper was to analyse the relationship of psychopathological and clinical variables with neuropsychological characteristics of patients with EDs and to determine possible influence of these variables on patients' attitude towards change.

Methods: An observational analytical cross-sectional study was performed. The participants were 74 consecutive outpatients who received treatment at an ED unit during a 6-month period. They were assessed using clinical (Psychiatric Status Rating Scale, modified) and neuropsychological tests (Letter Number Sequencing test; Stroop test; Symbol Digit Modalities Test; Rey-Osterrieth Complex Figure Test). They were asked to complete several self-report psychopathological questionnaires (Body Shape Questionnaire; Eating Disorders Inventory; Beck Depression Inventory; State-Trait Anxiety Inventory; Dissociative Experiences Scale; Attitudes Towards Change in Eating Disorders Scale), but 23 participants (31.08%) did not return them. Descriptive statistics and multivariate analysis were performed to study the relationships between clinical and psychopathological neuropsychological variables.

Results: Nineteen patients (25.68%) were diagnosed with restricting anorexia nervosa (AN), 19 (25.68%) with purging AN, 14 with bulimia nervosa (18.92%), 9 with binge eating disorder (12.16%) and 13 with ED not otherwise specified (17.57%). There were no significant differences among the groups in the scores on neuropsychological tests.

BMI was related to the majority of the neuropsychological scores. "Precontemplation" was related to copy time ($B=3.56$; 95% CI (0.82-6.29), $p<0.01$) and memory time ($B=-2.31$; 95% CI (-4.58-(-0.05)); $p<0.05$). "Contemplation" was related to copy time ($B=1.43$; 95% CI (0.42-2.45); $p<0.01$) and style ($B= -14.01$; 95% CI (-24.98-(3.04)); $p<0.01$). "Decision" was related to working memory (SpanLN), the quantitative copy score, order and style.

Conclusions: In EDs, neuropsychological dysfunction could be associated with decreased motivation to change. Hence, a comprehensive therapeutic framework should be established with the aim of providing neurocognitive training in addition to conventional therapy. This approach could enhance acknowledgment of the problem and improve the decisional balance.

Background

Plain English summary

Eating disorders (EDs) are prevalent and severe in the young population. The long-term dysfunction caused by EDs in a number of patients highlights the need for further research. Neurocognitive deficits have been suggested as potential transdiagnostic features that might contribute to the outcome of EDs. Executive functioning includes the cognitive processes that allow individuals to regulate their emotion and adapt their

behaviour according to their goals. Thus, improving executive functions, such as set-shifting and working memory, could help in treatment and functional recovery. There are a large number of publications about specific neurocognitive issues in EDs, mainly inhibitory control, decision making, central coherence, cognitive flexibility, attention bias, and working memory impairment. Several of these studies have also analysed the link between these neurocognitive issues and long-term outcomes. However, the relationship of neuropsychological features with the motivation to change has not been ascertained. The present work highlights the relevance of some specific neurocognitive process together with specific ED psychopathology related to change because a more controlling and less flexible attitude is associated with reduced motivation.

Multiple risk factors are related to the clinical course of EDs (1). Moreover, up to half of ED patients do not maintain diagnostic stability (2), which makes it difficult to establish a standardized therapeutic approach. The fact that up to 50% of patients experience a change in diagnosis indicates some common vulnerability (3). A transdiagnostic perspective that considers possible endophenotypes and subphenotypes of EDs could aid in the understanding of this variability (4) and inform a common therapeutic approach (5).

Neurocognitive deficits have been considered potential transdiagnostic mechanisms that contribute to psychopathology (6). At present, different studies have been carried out regarding neuropsychological aspects in EDs (7,8). Several of them have focused on a single diagnostic category or neurocognitive domain (9). Endophenotypic features of EDs have been identified in bulimia nervosa (BN) and anorexia nervosa (AN) (5,10,11). Research models have attempted to identify relationships among the neuropsychological dimensions, psychopathological disturbances and clinical manifestations of EDs (12).

Among the neuropsychological variables that might play a relevant role in EDs are impairment in the ability to focus attention on target stimuli in the presence of distractors, cognitive inflexibility and weak central coherence (13,14). Sustained, inhibitory or selective attention in patients with BED (binge eating disorder) shows variable results in AN and BN (15–21). Additionally, studies have found increased interference in Stroop's test when words related to the body are used (21,22), although this interference was not specifically related to psychopathological disorders, such as drive for thinness or body dissatisfaction (15,23). Memory has also been shown to be impaired in BED and has been related to the frequent comorbidity of depressed mood symptoms (8) and length of illness.

Executive functioning is responsible for the control of such cognitive processes as setting goals, planning and organizing. One indicator of executive functioning, set-shifting, involves the ability to observe and respond to changes in rules and move back and forth between tasks, operations or sets (24). Impaired ability in this area is postulated to contribute to rigid and obsessive behaviour. It is moderately heritable, and deficits have been shown in both women with AN and women with high levels of obsessiveness who have no history of EDs. Interestingly, these set-shifting deficits persist after recovery from AN. Set-shifting appears to be among the most interesting endophenotype candidates (11). Thus, cognitive inflexibility (that is to say, the lack of alternatives for dealing with everyday problems) could be a feature of EDs associated with perfectionism (9,25–27), or a trait that could be considered a phenotype (28). On the other hand, weak central coherence (namely, global processing difficulties with increased local processing, i.e., excessive attention to detail) such as overvaluation of body image in opposition to a superior sense of self (13,14) has also been pointed out as a

characteristic of AN (54). These neuropsychological factors -set-shifting and weak central coherence - would likely make more difficult for patients to develop new cognitive and behavioural skills and could influence their outcomes (54).

A variable that interferes with the outcome of EDs is attitudes towards change (29,30), which might mediate the effect of another psychopathological variables, such as age at onset and nutritional status (31,32) The transtheoretical model of change defines phases that serve as an index of the patient's motivational state to identify where each subject is regarding changing his/her disease behaviour (33). To make therapy more effective, the therapist helps the patient identify the change phase of each problem behaviour and adapts his/her interventions accordingly. In this setting, patients achieve the ability to determine their own pro and cons to shift the decisional imbalance towards change, and neurocognitive functions are critical for this task. Further longitudinal research may help to determine whether neurocognitive deficits also influence attitudes towards therapeutic change. If that is the case, neuropsychological rehabilitation would have some complementary utility in promoting change (7,34,35). There is less evidence regarding rehabilitation in EDNOS and BN. Although cognitive inflexibility has been replicated in these patients (22), major studies of cognitive remediation in ED have not been carried out with AN (36). However, neurocognitive treatments seem to be useful for treating EDs and weight disorders (37).

In summary, taking into account that cognitive inflexibility and weak central coherence could contribute to the perpetuation of EDs, thus hindering the motivation to change (38–42), it would be interesting to conduct neuropsychological assessments in addition to psychopathological assessments and measurements of attitudes towards change at the beginning of the treatment. The main objective of the present paper was to analyse the possible relationship between the neuropsychological characteristics of patients diagnosed with an ED and psychopathological and clinical variables and to determine the possible association of these characteristics with patients' attitude towards change.

Methods

A cross-sectional observational analytical study was performed. The participants were women who consecutively presented for treatment at the Eating Disorders Outpatient Unit of General University Hospital of Ciudad Real during a 6-month period. Inclusion criteria were (1) diagnosis of anorexia nervosa (AN), bulimia nervosa (BN), binge eating disorder (BED) or eating disorder not otherwise specified (EDNOS) according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5); (2) female gender; (3) age between 18 and 50 years; (4) a current clinical state that permitted psychometric evaluation. Comorbid symptoms of depression and anxiety were permitted. Patients were excluded if they 1) spoke a native language other than Spanish; (2) did not give written informed consent; (3) were male; (4) had comorbid bipolar disorder, psychotic disorder, major depressive disorder, organic mental disorder, attention-deficit hyperactivity disorder, autism spectrum disorder, Tourette syndrome or chronic fatigue syndrome.

Participants

At the beginning of the study, 74 patients were included. The mean age was 28.97 years (standard deviation, SD, 9.30). The participants were informed about the procedure, and those who agreed to participate signed the informed consent. Clinical assessment and neuropsychological tests were administered, and the participants

were given psychopathological self-report questionnaires to complete. Twenty-three participants (31.08%) did not return the questionnaires.

Although the sample was finally reduced to 51 subjects for most of the psychopathological variables, neuropsychological and clinical features could be evaluated in the 74 patients who were initially included. When the patients who did not return the questionnaires were compared to the ones who did, no differences were found regarding age, body mass index (BMI), age at onset, course of the disorder, education level, use of drugs, diagnoses, compensatory symptoms or neuropsychological scores.

Procedure

All patients who participated in the study were offered one year of treatment. This included twelve personal sessions of motivational enhancement therapy, six psycho-educational group sessions and twenty cognitive-behavioural therapy sessions. Treatment was based in Fairburn's program (43) with 20 50-minute sessions based on enhanced cognitive behaviour therapy. Pharmacological treatment was provided when necessary.

Each day, selected patients were informed about the study and its procedure, and informed consent was obtained. After this, the self-report questionnaires were provided. Maximum confidentiality was guaranteed by removing any identifying information from the patients' clinical data and storing data in a password-protected Excel base. The local Clinical Research Ethics Committee approved the study.

Instruments

All psychopathological tests were given to the patients to complete at the hospital while they waited for their appointment. The evaluation started with the Letter Number Sequencing test, followed by the Stroop test, the Symbol Digit Modalities Test and the copying portion of the Rey-Osterrieth Complex Figure Test (ROCF). As it was necessary to wait five minutes before performing the drawing from memory task, the clinical questionnaire was given to the patients after the figure copying task; when the questionnaire was completed, the patients were asked draw the complex figure from memory.

Clinical test:

Clinical interview

A clinical interview was completed to collect information about symptoms, body parameters, exclusion and inclusion criteria and diagnoses and to obtain data regarding age at onset and education level (necessary for neuropsychological evaluation).

Status

The patient's clinical status was evaluated by the Psychiatric Status Rating Scale. This scale is based on Herzog's work (30) and was updated with the DSM-5 criteria for the different disorders. Clinical status was divided into three groups, each of which included two different categories: scores of 5-6 indicated that the patient met the criteria for the disorder ("Definite criteria, severe" and "Definite criteria"); scores of 3-4 indicated partial recovery ("Marked" and "Partial remission"), and scores of 1-2 indicated total recovery ("Residual" and "Usual self"). Afterwards, to improve statistical power, these categories were combined to create a

dichotomous variable: “No evidence of illness” (Usual self, Residual, Partial remission) and “Evidence of illness” (all other categories). The original scale is included in additional file 5.

Psychopathological tests:

Body Shape Questionnaire (BSQ).

The BSQ was validated for the Spanish population by means of a 34-item self-report questionnaire with a six-point Likert-style rating scale (1= never; 6= always) (44). It measures concerns about body weight and shape in ED. Its internal consistency using Cronbach's index is good (0.97), as is its concurrent validity. It differentiates clinical from nonclinical subjects and people with more or less concern about their weight. A score of 105 is the cut-off point for the Spanish population (44).

Eating Disorders Inventory (2nd edition) (EDI-2).

The EDI-2 is a self-report questionnaire with 91 items (11 scales: “Drive for thinness”, “Bulimia”, “Body dissatisfaction”, “Ineffectiveness”, “Perfectionism”, “Interpersonal distrust”, “Interoceptive awareness”, “Maturity fear”, “Ascetism”, “Impulsiveness” and “Social insecurity”). The internal consistency (Cronbach's alpha) is higher than 0.80 in ED samples. Reliability coefficients (alpha) were from 0.83 to 0.93 in samples of patients from the original studies. The EDI-2 is validated for the Spanish population (45,46).

Beck Depression Inventory (BDI).

The BDI is a self-reported questionnaire with 21 items for evaluating the existence and severity of depressive symptoms. Its internal consistency is higher than 0.85 (47,48).

State-Trait Anxiety Inventory (STAI).

The STAI is divided in two independent scales that measure state and trait anxiety. Cronbach's alpha is 0.90 for trait anxiety and 0.94 for state anxiety (49–51).

Dissociative Experiences Scale (DES).

The DES is a self-assessment questionnaire based on a visual analogue scale composed of 28 dissociative experiences; it asks how often the subject experiences these dissociative events (0-100%). An average score of 30 or more indicates that dissociative disorder is expected (52–55). The DES comprises 3 scales: “Derealization and depersonalization”, “Absorption” and “Amnesia” (56). Its internal reliability (Cronbach's alpha) is 0.93, and its retest-reliability is 0.87 (56).

Attitudes Towards Change in Eating Disorders Scale (ACTA).

The ACTA, a Spanish validated self-report questionnaire with 59 items, was used to evaluate the attitudes towards change in cognitive, affective, behavioural, and relational features in ED patients (46). It is based on Prochaska and DiClemente's theoretical model concerning the phases of change (57). The ACTA comprises 6 scales: “Precontemplation”, “Contemplation”, “Decision”, “Action”, “Maintenance” and “Relapse”. The “Precontemplation” subscale refers to the refusal to consider the presence of a disorder. The “Contemplation”

subscale reflects a state in which the subject recognizes his/her eating problem, although he/she may underestimate its importance and shows no motivation to change his/her behaviours. The "Decision" subscale reflects that the patient has decided on a date at which he/she will begin to make changes. The "Action" subscale shows evidence of change in different areas: cognitive (positive thoughts about the resolution of the disorder), behavioural (changing habits for other, healthier ones), and affective (the patient perceives the disorder as an unpleasant problem that must be modified). The "Maintenance" subscale evaluates the stability of the achievements obtained in the action phase. Finally, the "Relapse" subscale is a subjective assessment of any worsening that the subject may experience. The reliability of each scale is from 0.90-0.74, and their retest-reliability ranges from 0.86-0.64 (46). It is designed for ED patients. An additional file describes the scale in greater detail [see Additional file 1] (in this study, the Spanish version was used).

Neuropsychological variables:

Working memory

This variable was measured using the Letter Number Sequencing test (LNS III) included in Wechsler Adult Intelligence Scale (WAIS-III) (58). For this test, participants listen to verbal sequences of letters and numbers that gradually increase in length and must be memorized, ordered and repeated back to the tester. The reliability and validity of this test are high, but the available data are related to intelligence evaluation. Two indexes are obtained: Total score and SpanLN.

Inhibitory attention

"Stroop's effect" (59) is defined as the difference in the processes of naming colours and reading words. It is examined using the Stroop test, which measures inhibitory attention. Test-retest reliability is high in all studies (0.69-0.89) (60). The test comprises three pages: Two of them represent the "congruous condition", in which participants are required to read the names of colours (henceforth referred to as colour words) printed in black ink (W) and to name different colour patches (C). On the third page, which represents the colour word (CW) condition, colour words are printed in an inconsistent colour of ink (for instance, the word "red" is printed in green ink). Thus, in this incongruent condition, participants are required to name the colour of the ink instead of reading the word. In other words, the participants are required to perform a less automated task (i.e., naming ink colour) while inhibiting the interference arising from a more automated task (i.e., reading the word). An additional file describes this test in more detail [see Additional file 2] (in this study, a Spanish version was used). The indexes obtained were W (the number of words read on the first page), C (the number of colours named on the second page), CW (the number of colours named on the third page) and interference. All these indexes are corrected by age.

Sustained attention

The Symbol Digit Modalities Test (SDMT) (61,62) mainly evaluates attention (included sustained attention) (63), optical tracking, speed of mental processing and visuo-motor speed. The test is based on the pairing of meaningless geometrical images with numbers from 1 to 9 according to a previous model. The indexes obtained are the total score and the scored SDMT (corrected by age and education level).

Executive function

The ROCFT (64,65) consists of copying a complicated line drawing and then drawing it from memory. Several indexes are obtained: quantitative and qualitative scores of copied and memorized reproduction accuracy (scored using Osterrieth's method, as explained in Additional file 4), style, order and central coherence (explained in Additional file 4) (66–69). A global approach, for example, is shown by a tendency to draw the main structural elements first and place local elements in relation to this framework. On the other hand, individuals may copy the figure by first drawing local details and failing to maintain their overall spatial organisation. An extreme piecemeal approach is often seen in very young children and individuals with right hemisphere damage, although healthy adults differ in the degree to which they use a local or global strategy. Scoring and the style, order and coherence indexes are explained in Additional file 4. The indexes obtained were copy and memory accuracy, copy and memory time, copy and memory type, order index, style index and central coherence index.

Data analysis

SPSS 19.0 was used to analyse the data obtained.

A descriptive analysis was performed, followed by an inferential analysis. The statistical level accepted as significant was 5% ($p < 0.05$). Qualitative variables were statistically analysed by means of the chi-square test for independence. Quantitative variables were examined for normal distribution using the Kolmogorov-Smirnov test if there were more than 50 data and the Shapiro-Wilk if there were fewer than 50 data points). Student's t-test and the Mann-Whitney U test were used for dichotomous independent variables, and ANOVA and the Kruskal-Wallis test were used for independent variables with more than two categories. Pearson's and Spearman's correlations were used for quantitative independent variables.

Multivariate analysis was performed using simple linear regression to evaluate models of quantitative dependent variables. The variables included in the models were those that were statistically significant in the bivariate analysis of our sample and those that were statistically significant in previous studies or were considered of interest for the current study due to their transdiagnostic meaning (e.g., BMI, dichotomous status, age at onset of ED, antidepressant use, benzodiazepine use, total DES score, anxiety, depression, Perfectionism score). Later, the models were simplified to improve their alignment.

Results

Clinical, psychopathological and neuropsychological characteristics

Nineteen patients (25.68%) were diagnosed with restricting AN, 19 (25.68%) with purging AN, 14 (18.92%) with BN, 9 (12.16%) with BED and 13 with EDNOS (17.57%). The mean age at onset was 16.62 (SD 6.54). The mean time of evolution of the illness was 12.35 years (SD 9.41). Regarding status, 38 patients (51.35%) had evidence of illness, and 36 (48.65%) had no evidence of illness at the time of consult. A total of 52.70% were being treated with a psychotropic drug. The main results are summarized in Table 1. No significant differences were found among the diagnostic groups concerning the duration of the disorder, time of onset or clinical status. A total of 73.70% of patients with purging AN were treated with pharmacotherapy, which was a statistically significantly higher proportion ($p < 0.05$) than in other groups of subjects.

Table 1: Qualitative clinical variables and their relationship with each clinical subtype

Variable	Total sample N=74 Fr (%) / mean (SD)	Restricting AN n= 19 Fr (%) / mean (SD)	Purging AN n=19 Fr (%) / mean (SD)	BN n=14 Fr (%) / mean (SD)	BED n=9 Fr (%) / mean (SD)	EDNOS n=13 Fr (%) / mean (SD)
Age at onset	16.62 (6.54)	17.05 (7.01)	15.79 (2.82)	18.14 (7.00)	11.89 (3.79)	18.85 (9.24)
Number of years with the disease	11.14 (9.32)	10.95 (9.48)	13.00 (10.60)	10.21 (7.83)	21.44 (9.82)	9.46 (4.99)
Pharmacotherapy	52.70%	47.40%	73.70%*	42.90%	55.60%	38.50%
Clinical status						
NS	9 (12.20%)	2 (10.50%)	1 (5.30%)	2 (14.30%)	1 (11.10%)	3 (23.10%)
R	12 (16.20%)	2 (10.50%)	2 (10.50%)	2 (14.30%)	2 (22.20%)	4 (30.80%)
PR	15 (20.30%)	3 (15.80%)	3 (15.80%)	4 (28.60%)	2 (22.20%)	3 (23.10%)
M	11 (14.90%)	1 (5.30%)	3 (15.80%)	4 (28.60%)	3 (33.30%)	0 (0%)
DC	18 (24.30%)	6 (31.60%)	6 (31.60%)	2 (14.30%)	1 (11.10%)	3 (23.10%)
SC	9 (12.20%)	5 (26.30%)	4 (21.10%)	0 (0%)	0 (0%)	0 (0%)

NS: normal status; R: residual; PR: partial remission; M: marked; DC: defined criteria; SC: severe criteria; * $p < 0.05$
** $p < 0.01$ *** $p < 0.001$. Fr: frequency (χ^2 40.619, df 4). *** $p < 0.001$

Descriptive data of the neuropsychological variables are shown in Table 2. There were no significant differences among the diagnostic groups with regards to the scores on neuropsychological tests. However, when clinical status was considered, the copy time on the (ROCFT) was statistically significantly related to dichotomous status (Z -2.253, $p < 0.05$, mean 32.11 in patients who did not meet the criteria for disorder vs 42.61 in patients who met the criteria).

Table 2: Descriptive data for neuropsychological measurements

Variables	Mean	Median	SD
Quantitative variables			
Total LNS	18.18	18.00	2.79
SpanLN	4.80	5.00	0.94
W- corrected for age	100.97	108.00	26.43
C-corrected for age	75.49	74.50	11.26
CW- corrected for age	46.28	46.50	8.65
Interference	4.50	3.25	11.83
SDMT score	54.64	55.00	11.36
ROCFT copy time (min)	3.07	3.00	2.04
ROCFT copy quantitative (direct)	34.45	35.00	2.46
ROCFT memory time (min)	2.72	2.00	1.52
ROCFT memory quantitative (direct)	19.60	20.00	6.14
Order index	2.23	2.33	0.67
Style index	1.56	1.67	0.29
Central coherence index	1.45	1.52	0.32
Qualitative variables			
SDMT scaled score	Very low 8 (10.81%); Low 2 (2.70%); Normal 51 (68.92%); High 13 (17.57%)		
ROCFT copy types	I 46 (62.16%); II 10 (13.51%); III 5 (6.76%); IV 11 (14.86%); V 1 (1.35%); VI 1 (1.35%)		
ROCFT memory types	I 58 (78.38%); II 7 (9.46%); III 1 (1.35%); IV 5 (6.76%); V 1 (1.35%); VI 2 (2.70%)		
ROCFT observations	No observations 53 (71.62%); Completion 6 (8.11%); Poorness 5 (6.76%); Child/Perfectionism/Repeated lines/Very small/Unconnected 2 each (2.70%)		

LNS: Letter Number Sequencing; SpanLN: index of the Letter Number Sequencing test; W-, C-, WC-: indexes of the Stroop test; SDMT: Symbol Digit Modalities Test; ROCFT: Rey-Osterrieth Complex Figure Test; min: minutes; I..VI: types of performance on the ROCFT; SD: standard deviation

The descriptive data for psychopathological variables (Table 3) show that the highest mean scores on the ACTA were obtained on the "Action" subscale, followed by the "Relapse" subscale variable. The mean score on the BSQ was above the cut-off point of 105. Regarding the STAI, the mean "State" score was also above the (70) calculated mean score of 18.20, SD 11.62, for the Spanish population, and the average "Trait" score was 35.92, SD 13.26) (the average score for the Spanish population in the same work was 23.35, SD 10.6). The average DES score was 14.16, SD 15.17 (an average score over 30 points suggests the presence of a dissociative disorder).

Table 3: Variables of psychopathological tests

Variable	Mean	Median	SD
ACTA			
Precontemplation	10.73	10.00	8.46
Contemplation	16.42	16.36	9.34
Decision	17.22	17.27	94.41
Action	26.04	26.00	7.64
Maintenance	14.86	15.00	9.00
Relapse	17.51	15.71	11.37
EDI-2			
DT	11.61	12.00	6.77
B	3.61	3.00	5.23
BD	14.76	15.00	8.88
I	11.37	9.00	8.33
P	7.22	7.00	3.85
ID	5.86	5.00	4.44
IA	10.57	10.00	7.71
MF	8.78	6.00	6.22
A	6.49	5.00	5.00
IR	6.18	5.00	10.49
SI	8.65	9.00	5.69
BSQ	126.16	123.00	45.59
DES			
DES-amnesia	6.67	3.13	10.49
DES-absorption	22.66	21.11	21.63
DES- depersonalization	10.09	0.83	17.95
DES-total	14.16	8.93	15.17
BDI	20.88	22.00	10.34
STAI			
STAI-state	30.69	31.00	14.00
STAI-trait	35.92	35.00	13.26

DT: Drive for thinness; B: Bulimia; BD: Body dissatisfaction; I: Ineffectiveness; P: Perfectionism; ID: Interpersonal distrust; IA: Interoceptive awareness; MF: Maturity fear; A: Ascetism; IR: Impulsiveness; SI: Social insecurity.

Relationships between neuropsychological, clinical and psychopathological variables

When the neuropsychological variables were considered as dependent variables and the clinical and psychopathological variables were considered as independent variables or confounding factors in the multiple linear regression analysis, the models and variables within them that reached statistical significance ($p < 0.05$) are presented in Table 4.

Table 4: Multiple linear regression models (only significant variables)

Dimension	Dependent variable	Independent variable	B (CI)	p
Working memory	Total LNS	Depression	-0.26 (-0.38-(-0.14))	<0.001
		Dichotomous status	1.52 (0.11-2.92)	0.03
		BMI	0.13 (0.04-0.21)	0.004
	SpanLN	Depression	-0.07 (-0.11-(-0.03))	0.001
		Dichotomous status	0.66 (0.15-1.17)	0.01
		DES-total	0.02 (0.00-0.04)	0.04
Inhibitory attention	Interference	Perfectionism	1.07 (0.16-1.99)	0.02
		DES-absorption	0.41 (0.01-0.82)	0.04
Sustained Attention	SDMT score	Depression	-0.95 (-1.49-(0.40))	0.001
		STAI-trait	0.46 (0.42-0.88)	0.03
		Perfectionism	1.09 (0.31-1.87)	0.01
Executive functions	ROCFT time of copy	STAI-state	-0.04 (-0.08-0.00)	0.05
		BMI	-0.04 (-0.08-0.00)	0.06
	ROCFT copy quantitative	Age at onset	-0.11 (-0.21-(-0.01))	0.03
		Perfectionism	0.20 (0.01-0.40)	0.04
	Central coherence index	Antipsychotics use	0.59 (0.08-1.10)	0.02
		Antidepressant use	0.25 (0.05-0.46)	0.02
		Sedative-hypnotic use	-0.25 (-0.48-(-0.02))	0.03

B: beta coefficient; CI: 95% confidence interval; p: level of statistical significance; LNS: Letter Number Sequencing; STAI: State-Trait Anxiety Inventory; DES: Dissociative Experiences Scale; SpanLN: index of the LNS; SDMT: Symbol Digit Modalities Test; BMI: body mass index; ROCFT: Rey-Osterrieth Complex Figure Test.

Working memory

Regarding the total score on the LNS III, depression (as measured with the BDI), dichotomous clinical status and BMI were significantly associated ($p=0.002$, corrected $R^2=0.33$). In the model in which the SpanLN score was considered a dependent variable, the BDI score, dichotomous status and dissociation (DES total) were also significant ($p=0.006$, corrected $R^2=0.25$).

When the sample was limited to patients with AN and BN, BMI (standardized coefficient $B=0.43$; 95% $CI=0.05 - 0.81$; $p<0.05$ and corrected $R^2=0.12$) was the variable most strongly associated with the total LNS score.

Inhibitory attention

In the model in which interference was considered a dependent variable, the “Perfectionism” subscale score and the DES (“Absorption” subscale) were significant ($p=0.02$, corrected $R^2=0.19$). When only patients with AN and BN were considered, maturity fear was associated with interference scores (standardized coefficient $B=1.01$; 95% $CI=0.23 - 1.79$, $p<0.01$, corrected $R^2=0.30$).

Sustained attention

In the model in which the SDMT score was considered a dependent variable, the following variables were significant: BDI score, STAI-trait and “Perfectionism” ($p=0.001$, corrected $R^2=0.33$).

When only patients with AN and BN were considered, BMI was significant (standardized coefficient $B=1.79$; 95% CI=0.31 – 3.27; $p<0.05$; corrected $R^2=0.11$).

Executive function

When the copy time on the ROCFT was considered as a dependent variable ($p<0.05$, corrected $R^2=0.14$), none of the variables were significant, although the STAI-state score and the BMI were close to being statistically significant. In the model in which the copy score on the ROCFT was considered as a dependent variable, the significant variables were age at onset of illness and "Perfectionism" ($p<0.05$, corrected $R^2=0.26$). When the central coherence index was used as the dependent variable, the significant variables were the use of antidepressants, benzodiazepines, hypnotic sedatives and antipsychotics ($p<0.05$, corrected $R^2=0.15$).

Relationship between neuropsychological variables and attitude towards change

Copy time ($B=3.56$; 95% CI (0.82-6.29), $p<0.01$) and memory time ($B=-2.31$; 95% CI (-4.58-(-0.05)); $p<0.05$) were associated to "Precontemplation". "Contemplation" was related to the copy time ($B=1.43$; 95% CI (0.42-2.45); $p<0.01$) and style index ($B=-14.01$; 95% CI (-24.98-(-3.04)); $p<0.01$). "Decision" was related to working memory (SpanLN) ($B=-3.76$; 95% CI (-6.88 – (-0.64)); $p<0.05$), quantitative copy score ($B=1.31$; 95% CI (0.29-2.32); $p<0.05$), order index ($B=4.69$; 95% CI (0.29-9.09); $p<0.05$) and style index ($B=-17.06$; 95% CI (-28,08 – (-6,05); $p<0.001$).

Discussion

The main findings of the present work show that ED clinical subtypes do not significantly differ in terms of neuropsychological features. This might represent the transdiagnostic aspect of some neuropsychological dysfunctions in EDs related to emotional, cognitive and behavioural factors. Overall, there is a relationship between some neuropsychological test results and certain clinical characteristics, mainly BMI, age at onset, time of evolution of the disorder and clinical status. Psychopharmacological treatment might be considered as a confounding factor. Regarding psychopathological features, there is some association of perfectionism with sustained attention, interference and some executive functions, such as planning ability, as evaluated with the ROCFT copy score. In addition, executive function might influence attitude towards change. Being in the precontemplative, contemplative or decision stage is linked with executive functioning, especially in terms of copy time on the ROCFT test and working memory. Failures of executive functioning might lead to serious difficulties with planning and performing analyses of medium-long term consequences. Moreover, the above mentioned problems and lower capacity for insight usually present when patients are not ready to change. These results are relevant because of the possible influence of neuropsychological rehabilitation on functional recovery. Furthermore, the assessment of EDs along dimensional terms, as performed in the present study, helps to clarify that the neuropsychological features are not specific to diagnostic categories.

Neuropsychological features of ED and related clinical and psychological factors

Attention.

Inhibitory attention, assessed by interference on the Stroop test, was higher than expected (mean=4.50, $\sigma=11.83$ versus an expected score of 2.71, $\sigma=9.05$) (60). Furthermore, sustained attention was preserved or high in 86% of the patients. The psychopathological characteristics most related to this variable in the present work are perfectionism, anxiety and depressive symptoms. Inhibitory attention has also been previously related to neuroticism and to a more controlling, less flexible attitude (71). Other authors have also related attentional disturbances to clinical variables (17,22,71). The interest of the present work is that a variable with a possible transdiagnostic value, such as perfectionism, is associated with sustained attention in addition to anxiety and depression.

Working memory and executive functioning.

Working memory was reduced in the patients in this study compared to the general population (an average SpanLN between 5.7-4.9 was expected, and an average of 4 was found). Other authors (71) who exclusively explored patients with an AN diagnosis, found even lower scores, which could be explained by the existence of some degree of worsening (71–73).

Together, clinical status, BMI, depression and total scores on dissociation had value for predicting working memory deficits. Previous work on the topic of working memory in ED has also considered factors such as comorbid pathology, clinical course and patient clinical status (74), which were included in our model (58). The inclusion of psychopharmacological treatments would be considered a confusing factor. To date, we do not know of any study that has simultaneously considered all the factors that were analysed in the model.

The theoretical framework of working memory has been widely delineated; working memory can be defined as “the holding mechanism in the mind for keeping a small amount of information in a temporarily heightened state of availability” (21). It contains not only what we think of as the conscious mind, but also any other on-going processing and temporary memory functions outside of conscious awareness. Cognitive-emotional interactions may influence this process (75). Therefore, the negative emotional state of people with EDs could interfere with working memory.

Regarding executive functioning, cognitive inflexibility, the need for control in matters related to food and the difficulty of developing alternatives for managing everyday problems are common characteristics of people with EDs related to perfectionism (35). All this has led to the proposal of the possible deficits in the paradigms of change in the criteria, including the exploration of executive function (25,27). The instrument used in this paper, the ROCFT, is a complex test with multiple indexes whose quantitative and qualitative assessments provide interesting information (64). Its results show a visuoperceptive deficit in some patients.

From a clinical point of view, the BMI had an inverse relationship with the copy and memory time on the ROCFT, which supports difficulties with executive processing in patients with a lower BMI. BMI has been suggested as a predictor of treatment outcomes in AN (76,77) and is the physical criterion most commonly used as an indicator (31,76,78). One possible interpretation is that both BMI and the number of years with the disease are confounding factors and that status is more relevant and could be related to certain psychopathological features of EDs. This could suggest the presence of a slowdown in the processing of information in patients with worse clinical status, as shown by decreased flexibility when performing

assessment tasks (13,17,23,28,79,80) compared to the general population, as well as a greater tendency to pay excessive attention to details and have difficulty with global integration (80–82).

Copying accuracy scores were higher than expected with respect to the reference population, a finding that seems to be related to perfectionism. However, the average score for drawing from memory was lower than that of the general population, probably due to deficits in nonverbal memory and poverty in visuospatial integration, as described in other ED studies (14,22,81).

Neuropsychological features associated with attitude towards change and dissociation.

Dissociation, together with depression and clinical status, predicted dysfunctions in working memory. These findings are consistent with the multidimensional model of emotional regulation, which outlines the role of neurocognitive process, specifically the ability to filter and gate information in working memory (23). This relationship of dissociation and working memory has special relevance in EDs. Dissociation, or the “disruption in the usually integrated functions of consciousness, memory, identity, or perception” (83), is associated with fragmented or inadequate encoding of memory. Dissociation plays an important role in EDs and is related to mood-modulation mechanisms (84). The process of “cognitive narrowing” probably prevents unpleasant meaningful thoughts and provides an escape from distressing self-awareness (84). However, in addition to decreased self-awareness, one potential secondary effect of dissociation in EDs is dysfunction in working memory and executive functioning. In addition to causing emotional deregulation, dissociation can hijack endogenous attention and interfere with cognitive control process (85). Consequently, this may restrict the patient's ability to deal with the long-term consequences of his or her behaviour and be related to decisional imbalance, with an apparent effect on motivational state.

Patients who did not believe that they had a problem - that is, those who remained in the “Precontemplation” phase - tended to need more time to perform complex cognitive processes that require more planning and coordination, as evaluated by the ROCFT. The same was true for patients who were in the “Contemplation” and “Decision” phases, which are stages representing less mobilization for change.

These findings highlight the fact that in patients with long-term EDs, it is crucial to perform an exhaustive assessment in order to create an appropriate therapeutic plan. Many patients remain unmotivated to change, and conventional cognitive behaviour treatment may not help. Additionally, motivational therapy may not be successful in people with deficits in executive functioning. It could be hypothesized that patients with higher levels of dissociation are more resistant to change behaviour and also have worse neuropsychological functioning. Therefore, comprehensive integrated therapy is needed that includes a focus on emotional self-awareness, acceptance and effective neuropsychological training (23). The aim should be to identify and plan objectives and decisions that promote enduring changes.

Limitations

Some limitations deserve special mention, such as the cross-sectional nature of the study, which makes it impossible to elucidate whether the neurocognitive deficits are endophenotypic, that is, whether they existed prior to the psychopathology and will persist after recovery. Furthermore, the sample size was small considering the heterogeneity of the population studied and the 30% of the sample that did not complete all the

questionnaires. The absence of statistically significant differences between the people who did and did not complete all the tests suggest that abandonment was not related to neuropsychological variables or the patients' clinical situation.

The relationship between psychotropic drug use and attention and cognitive speed, as well as the fact that patients taking psychotropic drugs are generally those with the greatest comorbidity or risk, lead to the consideration of this factor as a possible confounder in the study. Other unfavourable effects of the presence of depressive symptoms at the beginning of therapy on executive function have been described in other studies (7).

Conclusions

Neuropsychological dysfunction in the population studied and its relationship with certain factors that are considered precipitating or maintaining underline the importance of neuropsychological evaluation in people with EDs. These alterations could be summarized as reduced working memory and increased interference compared with the general population. Resistance to change was also associated with more controlling and less flexible neuropsychological functioning.

Clinical impact and future lines of study

The overall analysis of the sample shows promising results regarding the relationship between dysfunction in some executive functions, especially central coherence, and EDs, as indicated in previous studies. The findings of the present study also support the transdiagnostic perspective, since the participants' DSM-5 diagnosis was not as relevant as other clinical variables related to the duration of the disorder.

The findings indicate that factors related to excessive attention to detail, the loss of a global perception of the situation and the capacity for attention maintenance correspond to variables related to greater therapeutic resistance, reflecting the low benefit of traditional cognitive behavioural techniques. Evaluation from a holistic perspective is necessary to allow the incorporation of cognitive rehabilitation into treatment.

List Of Abbreviations

Attitudes Towards Change in Eating Disorders Scale ACTA

Anorexia nervosa AN

Beck's depression inventory BDI

Binge eating disorder BED

Body Mass Index BMI

Body Shape Questionnaire BSQ

Bulimia nervosa BN

Bulimic Investigatory Test, Edinburgh	BITE
Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition	DSM-5
Dissociative Experiences Scale	DES
Eating disorders	ED
Eating Disorders Inventory	EDI
Eating disorder not otherwise specified	EDNOS
Letter Number Sequencing	LNS
Rey-Osterrieth complex figure test	ROCFT
State-Trait Anxiety Inventory	STAI
Symbol and Digit Modalities Test	SDMT
Wechsler Adult Intelligence Scale	WAIS

Declarations

Ethics approval and consent to participate: Informed consent was signed and Local Clinical Research Ethics Committee (Hospital General Universitario from Ciudad Real) approved the study.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions: BMS collected, analysed and interpreted the patient data. LBF and TRC supervised every part of the investigation work and were contributors in writing the manuscript. VMM contributed in writing and translating the manuscript. All authors read and approved the final manuscript.

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Additional File Legends

Additional file 1.doc. ACTA. Complete Attitudes Towards Change in Eating Disorders Scale in English.

Additional file 2.doc. Stroop Test. Complete Spanish Stroop Test (authors don't have English version).

Additional file 3.doc. Complete Symbol Digit Modalities Test.

Additional file 4.doc. Rey-Osterrieth Complex Figure Test. Explanation of indexes including Booth's indexes.

Additional file 5.doc. Complete Psychiatric Status Rating Scale.

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