Available online at www.sciencedirect.com

SciVerse ScienceDirect

Comprehensive Psychiatry 52 (2011) 587–595

Comprehensive PSYCHIATRY

www.elsevier.com/locate/comppsych

Neuropsychological psychopathology measures in women with eating disorders, their healthy sisters, and nonrelated healthy controls

Michal Hason Rozenstein[a,b,*], Yael Latzer[a,b], Daniel Stein[c], Zohar Eviatar[a]

[a]*University of Haifa, Rambam Medical Center, Ha' Alia Hashnia 2, Haifa, Israel*

[b]*Rambam Medical Center, Haifa, Israel*

[c]*Sheba Medical Center, Tel Hashomer, affiliated with the Sackler Faculty of Medicine, University of Tel Aviv, Israel*

Abstract

Objective: To assess the familial influence on neuropsychological dysfunction in eating disorders (ED) patients by comparing 16 patients with restricting type anorexia nervosa (AN-R), 18 patients with bingeing purging type anorexia nervosa, 20 patients with bulimia nervosa binge-purge type, 21 of the patients' nonaffected sisters, and 20 nonrelated healthy controls.

Methods: Self-report questionnaires assessing psychopathology and 2 computerized cognitive tasks measuring hemispheric asymmetry for language and visuospatial abilities were administered to all participant groups.

Results: On the self-report questionnaires, ED patients scored significantly more pathological than the healthy controls, whereas the healthy sisters were similar to the nonrelated healthy control group. For both of the computerized tasks, the behavior pattern of the sisters was similar to that of all, or most ED groups, and were significantly different from the nonrelated healthy controls. In addition, AN-R patients performed significantly worse on the visuospatial task than the other ED groups.

Conclusions: The dissociation between the performance on the cognitive tasks and psychopathology measures in healthy sisters, when compared to the ED and nonrelated healthy control groups, suggests that disturbances in neurocognitive functioning in ED patients are not necessarily the result of ED-related dysfunction. Rather, this may indicate general individual differences in cognitive processes that may run in families irrespective of the ED condition of the family member. The findings, with respect to the AN-R patients, support a neurocognitive continuum model of EDs in which AN-R represents the most severe form of the illness.

Eating disorders (EDs) represent highly complex bio-psycho-socio disturbances, likely reflecting interdependent interactions of antecedent genetic, biological, psychological, familial, and sociocultural parameters [1]. In recent years, there is growing interest in the role of neuropsychological dysfunction in the predisposition to an ED. Extensive reviews of neuropsychological functioning in women with EDs note that there are deficits in impulsivity, attention, visuospatial processing, concept formation, problems solving, and psychomotor speed [2,3].

Accordingly, patients with both anorexia nervosa (AN) and bulimia nervosa (BN), have been found to show an attention bias with respect to specific eating-related stimuli, usually those associated with body weight and shape. These difficulties in attention control have been found in a variety of neuropsychological tests, including the Stroop, Tower of London, the Wisconsin card sorting test, and Ray Complex Figure. In addition, disturbances in visuospatial tasks, particularly those associated with body size estimation [4], but also in non-ED related spatial tasks [5], have also been found to occur to a greater extent in ED vs non-ED control participants. Lastly, difficulties have been found in patients with ED in a variety of set-shifting tasks, a finding that has been interpreted as indicating a deficit in working memory [6-12].

Previous studies have further suggested that hemispheric functioning may be abnormal in ED patients with respect to both specific and general domains. Smeets and Kosslyn [13] found that patients with AN may judge images of their own body, but not of other women as fatter when these images are projected to the left hemisphere (LH) but not to the right hemisphere (RH). According to Bradley et al [14], patients with AN do not show the expected right/left electrophysiological asymmetry in an emotionally free verbal task (ie, a right

* Corresponding author.

E-mail addresses: michalhason@gmail.com, m_hason@rambam.health.gov.il (M.H. Rozenstein).

0010-440X/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.comppsych.2011.01.006

visual field [RVF] advantage for verbal tasks). Lastly, Eviatar, Latzer, and Viksman [15] found that ED patients show anomalous lateral dominance patterns in neutral verbal and spatial tasks.

It is still unclear whether these cognitive abnormalities are related to a genetic vulnerability, are secondary to the disturbed consummatory patterns of ED patients, or represent an interaction of both factors. One means to understand the source of these neurocognitive findings is to assess them among women who share some genetic and environmental vulnerability with the ED patients but, unlike them, do not have the illness, namely, their healthy sisters.

With respect to ED patients, their first-degree relatives may present not only with elevated rates of EDs [16,17] but also with higher levels of core ED-related personality attributes [18]. Moreover, not only patients with AN but also their healthy sisters have been recently found to show poorer performances on a variety of tasks investigating set-shifting [19] and central coherence [20].

In the present study, we attempted to assess the familial influence on neuropsychological dysfunction in ED patients by comparing patients with restricting type AN (AN-R), patients with bingeing purging type AN (AN-B/P), patient with BN, the patients' nonaffected sisters, and nonrelated healthy controls. We sought to examine patterns relevant to the functional architecture of cognitive neuropsychology, specifically those related to the issue of lateralized hemispheric functioning.

The participants performed a series of tasks designed to measure 2 types of cognitive tasks. Although previous studies have focused mostly on ED-related stimuli such as food or body shape, we used neutral stimuli, in line with the designs of Roberts et al. [19] and Tenconi [20], to control for the attentional bias likely created by ED related stimuli. We used 2 experimental tasks using the divided visual field paradigm. This technique takes advantage of the finding that stimuli presented in the left side of the visual field are initially processed exclusively by the RH, whereas stimuli presented in the right side of the visual field are initially processed exclusively by the LH. Although information is likely transmitted from one hemisphere to the other via the corpus callosum, the interpretation of divided visual field studies rests on the assumption that responses to stimuli presented briefly to one visual field reflect mainly the processing of that stimulus by the contra-lateral hemisphere, so that responses to targets in the RVF reflect LH processes and responses to targets in the left visual field (LVF) reflect RH processes (see Refs. [21,22]).

We used a lexical decision (LD) task, which is known to be preferentially performed in the RVF (reflecting LH processes), and a bar graph (BG) task, which is known to be preferentially performed in the LVF (reflecting RH processes). Thus, each task includes a modal pattern of normal performance asymmetry: a RVF advantage in the language task (the LD task) and an LVF advantage for the spatial task (the BG task) [23]. Discrepancies from the pattern expected in healthy controls may indicate deviations in functional hemispheric asymmetry. Participants also completed a series of self report questionnaires measuring relevant core ED personality traits.

The following are our hypotheses:

1. A main effect of group will be found in both the experimental tasks and in the self-report questionnaires. Specifically, significant differences will be found between the nonrelated healthy control group and the patient groups. If our measures tap a familial trait, we expect the sisters group to be more similar to the patient group and different from the nonrelated healthy control group. However, if our measures tap a specific effect of ED, we expect the sisters group to be more similar to the nonrelated healthy control group, and different from the patient group.
2. Whereas all ED groups would fare worse than both control groups in their spatial (but not verbal) functioning, patients with AN-R would be more disturbed in their neurocognitive functioning in comparison to patients with BN. This hypothesis incorporates Strober's finding that AN-R represent the most severe level of the disease with respect to neurocognitive functioning, BN the least severe and AN-B/P in between [17].

1. Methods

1.1. Participants

Ninety-five right-handed women participated in the study. Handedness was assessed using a modified version of the Edinburgh handedness questionnaire [24]. All women were native speakers of Hebrew with no diagnosis of learning disabilities or attention deficit hyperactive disorder. The participants were divided into 5 groups according to their main diagnosis: BN purging type (BN-B/P; n = 20), AN-B/P (n = 18), AN-R (n = 16), the ED patients' healthy sisters (n = 21), and a control group of age-matched nonrelated healthy women (n = 20). We did not include a group of BN non-purging type because during the year of the study, we diagnosed only one woman with this disorder.

Eating disorders participants were recruited from the outpatient ED clinic at the Rambam Medical Center, Haifa, and the adult and adolescent inpatient ED departments at the Sheba Medical Center, Tel Hashomer, Israel. No differences were found in any of the medical and psychological parameters assessed between inpatients and outpatients, or among patients from different treatment facilities. Accordingly, patients were grouped based on their specific ED subtype.

Nonrelated control participants included undergraduate psychology students from Haifa University, recruited by advertisements, and age-matched friends of the participants. No differences were found in any of the dependent variables

introduced between the 2 control populations. For their time and traveling expenses, the patients and their sisters received 75-150 NIS (matched to hospital policy). Nonrelated healthy control participants were rewarded with course credit or a present. Participants (and a parent if patients and controls were younger than 18 years) signed a written informed consent after receiving a detailed explanation about the aims and methods of the study. The study was approved by the Helsinki Committees of both medical centers.

The healthy sisters group included in the study consisted of 9 sisters of patients with BN-B/P, 5 sisters of patients with AN-R, and 7 sisters of patients with AN-B/P. In the case of multiple siblings, the healthy sister included in the study was the one whose age was closest to the ill sister. The sisters group was not matched according to the diagnosis of the ill sibling, because of the well-known lack of stability of any specific ED diagnosis and the potential to move to another diagnostic entity during the course of the illness [25]. In addition, several of the healthy sisters had another ill sister with another ED diagnosis than that of the ill sister included in the study. Lastly, due to the relatively small number of the healthy sisters included in the study, any further subdivision would be impractical for statistical reasons.

Patients with ED were assessed within 2 to 4 weeks of admission to the respective treatment facility when their medical and psychological condition was stabilized enough to be included in the study. Accordingly, although all patients with anorexia were underweight on admission, the weight of several patients was already greater at the time of assessment than required for the diagnosis of AN. Thus, when assessed, 11 patients with AN (6 with AN-B/P and 5 with AN-R) were still underweight (body mass index [BMI] <17 kg/m^2], whereas the BMI of 21 patients (12 patients with AN-B/P and 11 with AN-R) was already equal or above17 kg/m^2. Nevertheless, the use of *t* tests for unequal groups on all the dependent variables revealed no significant between-group differences in any of these parameters. Therefore, patients with AN were pooled according to their ED subtype (AN-R vs. AN-B/P), irrespective of their present BMI.

Participants were high school or university students, or graduated from high school without further schooling. No between-group difference was found with respect to education level ($P > .2$). Age and BMI data are presented in Table 1. BMI data for the ED groups was gathered from the patients' medical files if hospitalized, or by self report for nonhospitalized ambulatory patients, their sisters, and the control group. A significant group effect was found for BMI, $F_{4,89} = 14.78$, $P < .0001$. As expected, the use of Duncan post hoc tests revealed that the AN-B/P and AN-R groups had a significantly lower BMI than the 3 other groups, which did not differ from each other. No between-group difference was found for age ($P > .7$) (see Table 1).

1.2. Instruments

1.2.1. Diagnostic tools

The diagnosis of an ED in the participants (according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* [26] criteria), or the lack of an ED in the controls, was achieved with a structured interview based on the ED criteria of the Hebrew version [27] of the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* Axis I Disorders–Patient version (version 2.0) [28]. The participants were independently interviewed by psychiatrists, clinical psychologists, or clinical social workers, all highly experienced in the diagnosis and treatment of EDs. One control participant was excluded from the study for fitting the criteria for BN. None of the sisters reached the diagnostic criteria for an ED.

1.2.2. Self report questionnaires

1.2.2.1. Beck Depression Inventory. This 21-item scale measures self-reported depressive symptoms [29]. Participants rate items on a 4-point scale ranging from rarely (0) to often (3). Alpha Cronbach for the Hebrew version, given in this study was 0.94. The Beck Depression Inventory (BDI) has been previously used in ED patients [30], including in Israeli samples [31].

1.2.2.2. Plutchik Impulse Control Scale. This 15-item scale measures self-reported impulsivity on a 4-point scale ranging from never (1) to almost always (4) [32]. Cronbach α for the Hebrew version given in this study was 0.8. The Hebrew translation of the scale has been shown to have good psychometric properties [33].

1.2.2.3. Leyton Obsessional Inventory. This 20-item self-report scale describes characteristic obsessive-compulsive symptoms (such as checking or cleaning) on a 5-point scale ranging from no (0) to (4) the relevant symptom prevents me

Table 1
Age, BMI, and self-report questionnaires in ED and control participants

	Controls (n = 20)	BN (n = 20)	AN-B/P (n = 18)	AN-R (n = 16)	Sisters (n = 21)
BMI	21.68 (2.59)	21.72 (1.92)	17.78 (2)	17.87 (1.83)	21.64 (3.58)
Age	24.87 (7.76)	23.3 (7.51)	22.19 (5.3)	23.22 (10)	23.86 (8.06)
BDI	5.42 (4.73)	22.21 (16.68)	26.12 (10.70)	27.47 (15.80)	5.86 (5.26)
PICS	27.16 (5.09)	34.47 (8.50)	34.12 (6.97)	30.33 (5.85)	30.19 (5.34)
LOI	8.63 (5.09)	31.37 (18.44)	31.35 (13.22)	33.00 (19.85)	14.95 (8.6)
Total EDI-2	20.15 (20.06)	109.39 (21.47)	103.63 (36.98)	93.07 (44.53)	31.95 (21.47)

SDs are presented in parentheses.

from doing a lot of things and I spend a lot of time because of it [34]. Cronbach α for the Hebrew version, given in this study was 0.94. The Leyton Obsessional Inventory (LOI) has been previously shown to successfully distinguish between ED and healthy controls [35]. The Hebrew translation of the questionnaire has been found to have good psychometric qualities and to distinguish between women with subthreshold EDs and women with no EDs [36].

1.2.2.4. Eating Disorders Inventory [37]. This self-report Inventory includes 11 subscales relating to core ED features: drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, maturity fears, interoceptive awareness, asceticism, impulse control, and social insecurity. A total Eating disorders Inventory (EDI)-2 can be constructed by adding the scores of all 11 separate sub-scales. The EDI-2 is widely used in ED research and diagnosis. Alpha Cronbach for the Hebrew version, given in this study was 0.93. The Hebrew version of the EDI-2 has been shown to successfully differentiate ED patients from healthy controls [31].

1.3. The lateralized experimental tasks

1.3.1. The BG Task

The stimuli were 6 BGs representing whole numbers from 1 to 6 [38]. The BGs appeared as vertical rectangles against horizontal reference lines at the 0, 4, and 8 levels. Each BG appeared 10 times in each visual field resulting in 120 experimental trials. The BGs subtend 1.8° × 5° of visual angle with the inner edge 2° off fixation. The center of the BGs was leveled with the fixation point. Each target BG was randomly paired with the others to form bilateral displays. A directional arrow appearing at fixation (< or >) indicated to the participant which visual field contained the target stimulus in a random sequence. Thus, a stimulus displayed on each trial consisted of a directional arrow in the center and two BGs, one in each visual field. The stimuli were composed of black lines on a gray background. The participants were asked to indicate whether the target BG represented an odd or an even number, by pressing 1 of 2 keys, the up arrow on the key pad to indicate "even" and the down arrow to indicate "odd." All responses were given with the right hand. The participants first performed a 24-trial practice set during which feedback was given about the correctness of the response (happy or sad face at fixation point). No feedback was given during the experimental trials. The participants were asked to respond as quickly and as accurately as possible. The 120 experimental trials were presented in four blocks of 30. Between the blocks the participants were allowed to rest. The length of these breaks was not controlled. An example of the sequence of events on each trial is illustrated in Fig. 1.

1.3.2. The LD task

The stimuli were 80 four-letter strings in unvoweled Hebrew, half of which were concrete words and half pseudowords presented in 2 blocks of 40 with a break in between. Forty words and pseudowords appeared in each visual field in random order. The stimuli were presented with their inner edge 1.5° of visual angle offset from fixation and subtended 2.5° to 3° of visual angle. Letter size was 0.5° × 0.5°.

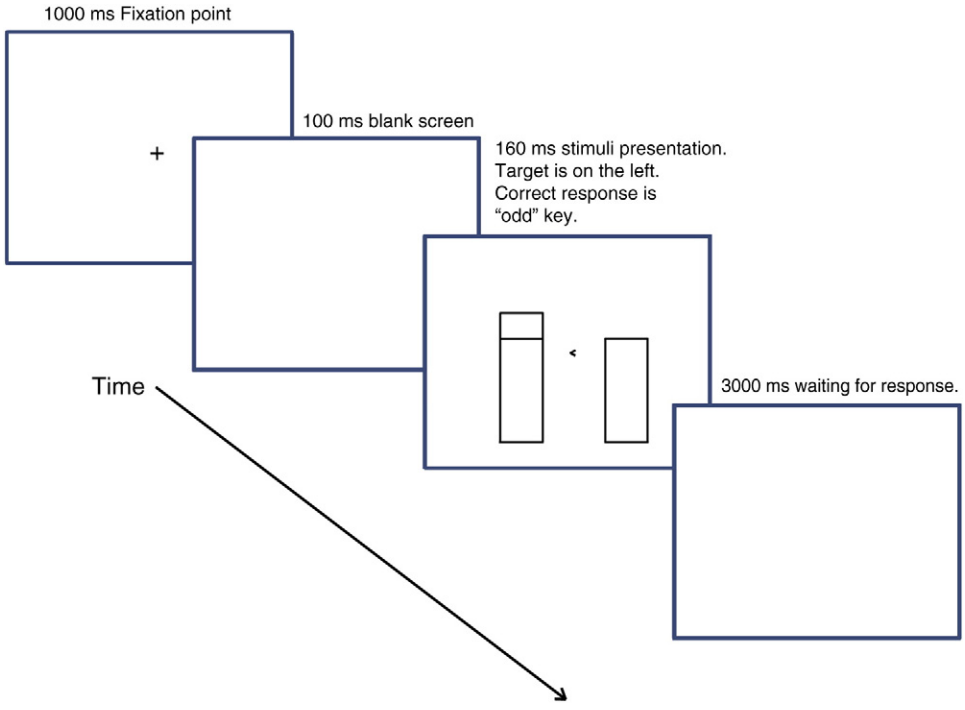


Fig. 1. Trial illustration, BG.

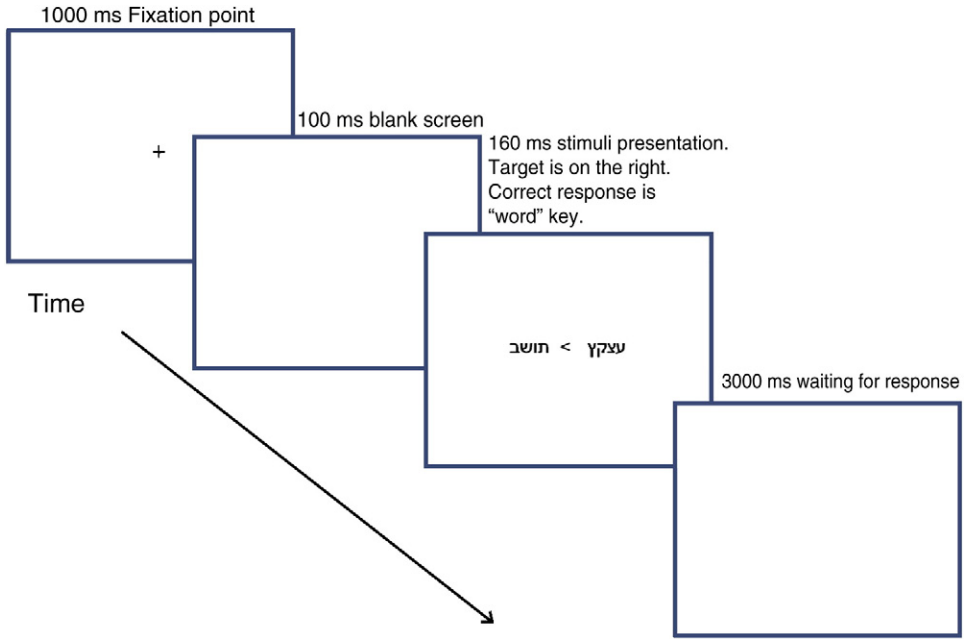


Fig. 2. Trial illustration, LD.

The stimuli were presented as black letters on gray background for 160 ms.

On each trial, one string was presented to each visual field with an arrow pointing to the target string, while the other string served as a distracter. Participants were given up to 3 s to respond, and the next trial began after 1 s. The task was to decide whether the string represents a familiar word in Hebrew or not by pressing a key. An example of the sequence of events on each trial is illustrated in Fig. 2.

2. Results

2.1. Self report questionnaires

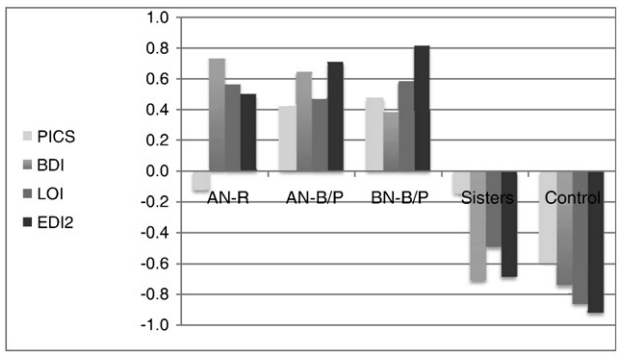
The scores of the participants on the self-report questionnaires were analyzed using the general linear model (GLM) procedure for unequal groups and Bonferroni comparisons between pairs of groups. Not all of the participants completed all questionnaires, so that the results reflect different group sizes. Table 1 describes the raw findings for the self- report questionnaires.

The between-group differences with respect to the self-report questionnaires are summarized in Fig. 3 (means have been transformed to z-scores in order to use the same scale).

The data show significant between-group differences for the BDI ($F_{4,90}$ = 16.58, P < .001), the LOI ($F_{4,90}$ = 13.16, P < .001), the Plutchik Impulse Control Scale (PICS) ($F_{4,90}$ = 4.13, P < .005), and total EDI-2 ($F_{4,88}$ = 8.66, P < .001). For the BDI, LOI, and total EDI-2 score, both control groups (healthy sisters and nonrelated healthy control) were different from all ED groups, whereas for the PICS, the 2 control groups were different only from the 2 B/P spectrum groups (P values for significant comparisons range between .001 and .0001). No differences were found between the sisters and nonrelated control group on any of the questionnaires.

2.2. Lateralized tasks: BGs and LD

The mean response time (RT) and % of error rate of the 95 women included in the study for both tasks were analyzed, using group (AN-R, AN-B/P, BN-B/P, controls, and sisters) as a between-groups factor, and task (BGs vs LD) and visual field (LVF, RVF) as within-subject factors. We used a GLM analysis for unequal groups. BMI was used as a covariate. Post hoc power analyses revealed that the observed power for RT was quite low: in the BG task, it was 0.24 for the LVF and 0.54 for the RVF; in the LD task, it was 0.35 for the LVF and 0.48 for the RVF. On the other hand, the observed power for



Legend: BN-B/P – bulimia nervosa bingeing/purging type; AN-B/P – anorexia nervosa bingeing/purging type; AN-R – anorexia nervosa restricting type; BDI - Beck Depression Inventory; PICS - Plutchik Impulse Control Scale; LOI - Leyton Obsessional Inventory; EDI-2 - Eating Disorders Inventory-2;

Fig. 3. Z scores of the group means on the PICS, BDI, LOI, and EDI2.

percentage of errors rate was quite high. Accordingly, in the BG task, it was 0.86 for the LVF and 0.87 for the RVF; in the LD task, it was 0.92 for the LVF and 0.98 for the RVF. This is reflected in the significant effects shown in the accuracy of responses vs the response times, as illustrated in Fig. 4.

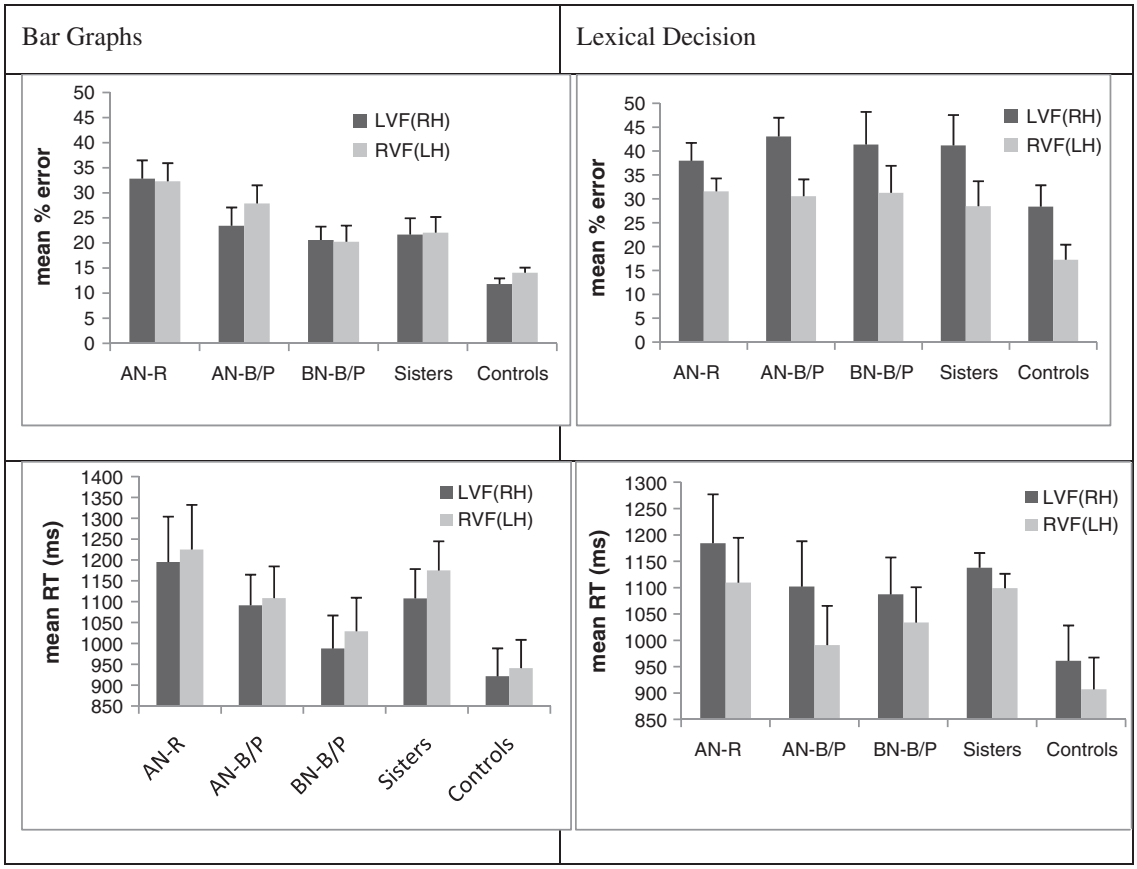
The overall GLM analysis revealed a significant interaction between visual field and task in both measures (RT: $F_{1,90} = 30.83$, $P < .001$; percentage of errors: $F_{1,90} = 51.29$, $P < .0001$). No other effects were significant for RT. The interaction of group with task was marginal for the error data, $F_{4,90} = 2.2$, $P = .07$. The main effect of task was significant for errors: $F_{1,90} = 50.93$, $P < .0001$, as was the main effect of visual field ($F_{1,90} = 28.39$, $P < .001$). The main effect of group was significant for the error measure, $F_{4,90} = 3.83$, $P < .05$. These patterns are described in Fig. 4 (error scores are in the top panels and RT scores are in the bottom panels, error bars are standard errors).

Several patterns can be seen in this figure. Importantly, all groups show opposing laterality patterns in the two tasks, and indeed, the simple interaction of task and visual field is significant in each group in errors and/or RT. Secondly, for both percentage of errors and RT scores, the sisters of ED women show patterns that are similar to the three patient groups, and different from the nonrelated control group. Lastly, the BG task performance in the AN-R group is generally worse in comparison to all other groups.

Planned comparisons of group differences in each of the conditions assess the patterns shown in Fig. 4. For the BG task, both AN groups fared worse than the nonrelated healthy controls in errors in both visual fields. Sisters were similar to both B/P spectrum groups and different from the controls in errors in the LVF, and in RT in the RVF. For the LD task, all patient groups fared worse than the nonrelated healthy controls in errors in both visual fields. Nonrelated controls were also different from the AN-R group in RT in both visual fields. Similar to the BGs task, sisters were not significantly different from any of the patient groups and were significantly different from the nonrelated controls in errors, in both visual fields and in RT in the RVF (P values range from .05 to .001). In addition, for the BG task, but not for the LD task, AN-R patients fared worse than both the BN-B/P and the sisters' group in errors in both visual fields ($P < .05$).

3. Discussion

The aim of the present study was to assess core ED traits and neurocognitive functioning in ED patients of different



Legend: BN-B/P – bulimia nervosa bingeing/purging type; AN-B/P – anorexia nervosa bingeing/purging type; AN-R – anorexia nervosa restricting type;

Fig. 4. Percentage of errors (top panels) and mean RT (bottom panels) in the BGs and LD tasks. Error bars are SEs.

subtypes, their healthy sisters, and nonrelated healthy control women. On the self-report questionnaires assessing depression, obsessionality, impulsivity, and core ED symptoms and attributes, ED patients scored worse than the healthy controls, whereas the healthy sisters were similar to the nonrelated healthy control group and different from all, or most, of the 3 patient groups. By contrast, for both neuropsychological experimental tasks, the behavior pattern of the sisters was similar to that of all, or most, ED groups, both being significantly different from the non-related healthy controls. No between-group differences were found with respect to hemispheric laterality patterns. In addition, our finding that the ED groups did not differ from each other on any of the personality questionnaires converge with those reported by Claes et al [39], who also found no clear association between categories of EDs and personality features, while using different measures of personality pathology.

These findings lead us to suggest that the most interesting finding of the study is the dissociation found among the healthy sisters, in contrast to the ill sisters, between their overall intact ED-related psychological condition, and their lower levels of neurocognitive functioning. These findings suggest that disturbances in language and spatial tasks in ED patients are not necessarily the result of ED-related dysfunction. The results converge with the findings of Karwautz et al [40], suggesting similar biological marks, but different personal vulnerability traits.

Our findings of significant differences between ED patients and non-ED controls (related and non related) on both the self-report questionnaires and the 2 neurocognitive tasks are in line with our first hypothesis. Thus, ED patients of different subtypes may perform less well than healthy controls on very basic spatial and verbal tasks based on disease-neutral stimuli. The healthy sisters, while being similar to the nonrelated healthy controls, and different from the patients, in showing no obsessionality, impulsivity, depression and core-ED attributes, do evince a neurocognitive deficit that is indistinguishable from the one shown by their ill sisters. These findings converge with other recent studies [19,20,41]. We believe that neurocognitive findings based on disease-neutral stimuli are especially informative, as they can indicate general individual differences in cognitive processes that may run in families, irrespective of the ED condition of the family member. By contrast, when specific ED-related spatial tasks are used, for example, Refs. [42,43], the pattern reported is of greater disturbance in ED patients vs their healthy sisters, who are found not to differ from unrelated controls, or from healthy relatives of control patients, respectively.

Our second hypothesis rested on Strober's continuum model of EDs with respect to neurocognitive dysfunction, where AN-R represents the most severe form and BN-B/P the least severe form of the disease. The results of the BG task support this hypothesis in that the performance of the AN-R group differs from all other groups except for the AN-B/P group. The decreased neurocognitive functioning of the AN-R patients is apparently not related to their low weight, as they are not different in this respect from the AN-B/P group. Nevertheless, there could be specific nutritional deficits in the AN-R group that are not present in the AN-B/P group because the latter do eat large quantities of food that may contain just enough nutrients to make some difference. The reduced abilities of AN-R patients are also probably not the result of greater disturbance in obsessionality, impulsivity or depression, as the scores of these patients in the self-report questionnaires are not different from the rest of the ED patients. As of yet we do not have an adequate explanation for this finding.

It is further notable that although the neurocognitive function of the AN-B/P group on both neurocognitive tasks is not different from the AN-R group, it is also not different from the BN-B/P and sisters groups. The standing of the AN-B/P patients in between the AN-R and the BN patients, lends further support to the continuum hypothesis of EDs [44,45]. This is most clear in Fig. 4, where a monotonic reduction is evidenced in RT and percentage of errors as we move from the AN-R group, through the AN-B/P group, to the BN-B/P group. Interestingly, the sisters break this monotonic trend, as they do not perform better, but rather worse or equal, than both binging/purging ED groups.

4. Limitations

Our study has several limitations. Firstly, our sample is relatively small, and some of the variance may be due to attention difficulties in the ED groups (although participants with attention deficit hyperactive disorder and other learning difficulties were eliminated from the study). Secondly, the experimental tasks were done in the participants' homes, their hospital surroundings, or in the research laboratory (this variation was not systematic). Thus, different testing conditions may have enlarged our error variance. Thirdly, the research population is not homogenous, coming from different inpatient and outpatient ED facilities. Nevertheless, the similarity found among inpatients and outpatients in all the parameters assessed, supports the notion that the discrepancies shown between ED patients and controls are not an artifact related to a specifically severe ED pathology. Lastly, as we have not related to the issue of comorbidity, some of the discrepancies between patients and controls might reflect an influence of a putative comorbid disturbance. Nevertheless, we have shown the presence of neurocognitive disturbances among healthy sisters of ED patients who have no elevated depression, impulsivity and obsessionality, as well as greater neurocognitive disturbance in the AN-R group despite being similar to the other ED patients in these psychopathological attributes. Accordingly, the neurocognitive disturbances found in our study are likely independent not only of the effect of the ED, but also of the ED-related comorbid conditions.

Our study has also some important advantages. Firstly, the inclusion of a specific sister control group has added to our understanding in showing that neurocognitive dysfunction in ED patients is not the mere result of the disturbed consummatory patterns per se. Secondly, we have used two different tasks tapping different aspects of neurocognitive functioning that are differently related to the issue of lateralized hemispheric functioning. In particular, the greater disturbance in the spatial task among patients with AN-R may emphasize the role of neurocognitive dysfunction in the highly elevated body image disturbances in these patients [4].

The field of neuropsychology among ED families is not yet developed. This study is one of the first studies directly dealing with neurocognition among healthy family members. There are many other elements that have not yet been investigated directly. Elements such as complex mental manipulations, visuographic abilities, decision making and social cognition among healthy family members. Better understanding of such neurocognitive patterns may help to understand the etiology of the disorder and focus family treatment.

5. Conclusions

There is still a controversy with respect to the clustering of characteristic ED symptoms and core ED personality traits in families of ED probands. Accordingly, whereas some studies have shown elevated levels of core ED characteristics in healthy parents [46,47], and sisters [18] of AN and BN patients in comparison to parents and sisters of controls, other studies [43], including ours, have failed to show such a discrepancy.

The study of factors potentially contributing to the development of an ED is hampered by the obvious difficulties inherent in prospective longitudinal examinations of premorbid populations [18]. One putative means to overcome these difficulties is the use of family-related designs [48,49]. Our findings that healthy sisters of ED women reveal similar patterns to ill participants in simple visuospatial tasks, support the notion that these disturbances may be present in ED patients well before the onset of the illness. Unfortunately, it is still too early to conclude that visuospatial derangements may have the potential to predispose to an ED. The difference found between the healthy and ill ED sisters in several core ED and personality related attributes suggests, on the other hand, that the trigger for the appearance of the illness may lie in these attributes, explaining why one sister in the family is healthy while the other one has developed an ED.

References

[1] Halmi KA. Eating disorders in females: Genetics, pathophysiology, and treatment. J Pediatr Endocrinol Metab 2002;15(5):1379-86.
[2] Duchesne M, Mattos P, Fontenelle LF, Veiga H, Rizo L, Appolinario JC. Neuropsychology of eating disorders: A systematic review of the literature. Rev Bras Psiquiatr 2004;26(2):107-17.
[3] Cook-Cottone C. Neuropsychology of eating disorders. The neuropsychology of women. New York (NY): Springer Science + Business Media; 2009. p. 175-207.
[4] Schneider N, Martus P, Ehrlich S, Pfeiffer E, Lehmkuhl U, Salbach-Andrae H. The assessment of body image distortion in female adolescents with anorexia nervosa: The development of a test for body image distortion in children and adolescents (BID-CA). Eat Weight Disord 2009;14(2-3):28-36.
[5] Fowler L, Blackwell A, Jaffa A, Palmer R, Robbins TW, Sahakian BJ, et al. Profile of neurocognitive impairments associated with female in-patients with anorexia nervosa. Psychol Med 2006;36(4):517-27.
[6] Brand M, Franke-Sievert C, Jacoby GE, Markowitsch HJ, Tuschen-Caffier B. Neuropsychological correlates of decision making in patients with bulimia nervosa. Neuropsychology 2007; 21(6):742-50.
[7] Mobbs O, Van der Linden M, d'Acremont M, Perroud A. Cognitive deficits and biases for food and body in bulimia: Investigation using an affective shifting task. Eat Behav 2008;9(4):455-61.
[8] Redgrave GW, Bakker A, Bello NT, Caffo BS, Coughlin JW, Guarda AS, et al. Differential brain activation in anorexia nervosa to fat and thin words during a Stroop task. Neuroreport 2008;19(12):1181-5.
[9] Roberts ME, Tchanturia K, Stahl D, Southgate L, Treasure J. A systematic review and meta-analysis of set-shifting ability in eating disorders. Psychol Med 2007;37(8):1075-84.
[10] Smeets E, Roefs A, Jansen A. Experimentally induced chocolate craving leads to an attentional bias in increased distraction but not in speeded detection. Appetite 2009;53(3):370-5.
[11] Smeets MA, Ingleby JD, Hoek HW, Panhuysen GE. Body size perception in anorexia nervosa: A signal detection approach. J Psychosom Res 1999; 46(5):465-77.
[12] Tchanturia K, Liao PC, Uher R, Lawrence N, Treasure J, Campbell IC. An investigation of decision making in anorexia nervosa using the Iowa gambling task and skin conductance measurements. J Int Neuropsychol Soc: JINS 2007;13(4):635-41.
[13] Smeets MA, Kosslyn SM. Hemispheric differences in body image in anorexia nervosa. Int J Eat Disord 2001;29(4):409-16.
[14] Bradley SJ, Taylor MJ, Rovet JF, Goldberg E, Hood J, Wachsmuth R, et al. Assessment of brain function in adolescent anorexia nervosa before and after weight gain. J Clin Exp Neuropsychol 1997;19(1): 20-33.
[15] Eviatar Z, Latzer Y, Vicksman P. Anomalous lateral dominance patterns in women with eating disorders: Clues to neurobiological bases. Int J Neurosci 2008;118(10):1425-42.
[16] Kaye WH, Devlin B, Barbarich N, Bulik CM, Thornton L, Bacanu SA, et al. Genetic analysis of bulimia nervosa: Methods and sample description. Int J Eat Disord 2004;35(4):556-70.
[17] Strober M, Freeman R, Lampert C, Diamond J, Kaye W. Controlled family study of anorexia nervosa and bulimia nervosa: Evidence of shared liability and transmission of partial syndromes. Am J Psychiatry 2000;157(3):393-401.
[18] Lilenfeld LR, Stein D, Bulik CM, Strober M, Plotnicov K, Pollice C, et al. Personality traits among currently eating disordered, recovered and never ill first-degree female relatives of bulimic and control women. Psychol Med 2000;30(6):1399-410.
[19] Roberts ME, Tchanturia K, Treasure JL. Exploring the neurocognitive signature of poor set-shifting in anorexia and bulimia nervosa. J Psychiatr Res 2010:40-50.
[20] Tenconi E, Santonastaso P, Degortes D, Bosello R, Titton F, Mapelli D, et al. Set-shifting abilities, central coherence, and handedness in anorexia nervosa patients, their unaffected siblings and healthy controls: Exploring putative endophenotypes. World J Biol Psychiatry 2010;11(6):813-23.
[21] Banich MT. Interaction between the hemispheres and its implications for the processing capacity of the brain. The asymmetrical brain. Cambridge (Mass): MIT Press; 2003. p. 261-302.
[22] Coulson S, Federmeier KD, Van Petten C, Kutas M. Right hemisphere sensitivity to word- and sentence-level context: Evidence from event-

related brain potentials. J Exp Psychol Learn Mem Cogn 2005;31(1): 129-47.
[23] Eviatar Z. Language experience and right hemisphere tasks: The effects of scanning habits and multilingualism. Brain Lang 1997;58(1): 157-73.
[24] Oldfield RC. The assessment and analysis of handedness: The Edinburgh inventory. Neuropsychologia 1971;9(1):97-113.
[25] Fichter MM, Quadflieg N. Long-term stability of eating disorder diagnoses. Int J Eat Disord 2007;40:S61-6.
[26] American Psychiatric Association Committee on Nomenclature and Statistics. Diagnostic and Statistical Manual of Mental Disorders (*DSM-IV*). 4th ed. Washington, DC: American Psychiatric Association; 1994.
[27] Shalev AY, Abramowits MZ, Kaplan de-Nour A. Structural clinical interview for axis I, *DSM-IV* disorders, Hebrew version; 1996.
[28] First MB, Spitzer RL, Williams JBW, Gibbon M. Structured clinical interview for *DSM-IV* (SCID). Washington, DC: American Psychiatric Press; 1995.
[29] Beck AT. The Beck depression inventory II. San Antonio: Harcort Brace; 1996.
[30] Pollice C, Kaye WH, Greeno CG, Weltzin TE. Relationship of depression, anxiety, and obsessionality to state of illness in anorexia nervosa. Int J Eat Disord 1997;21(4):367-76.
[31] Yackobovitch-Gavan M, Golan M, Valevski A, Kreitler S, Bachar E, Lieblich A, et al. An integrative quantitative model of factors influencing the course of anorexia nervosa over time. Int J Eat Disord 2009;42(4):306-17.
[32] Plutchik R, Van Praag H. The measurement of sociality and impulsivity. Prog Neuropsychopharmacol Biol Psychiatry 1989;13:S23.
[33] Horesh N, Orbach I, Gothelf D, Efrati M, Apter A. Comparison of the suicidal behavior of adolescent inpatients with borderline personality disorder and major depression. J Nerv Ment Dis 2003;191(9):582-8.
[34] Cooper J. The Leyton Obsessional Inventory. Psychol Med 1970;1: 48-64.
[35] Tokley M, Kemps E. Preoccupation with detail contributes to poor abstraction in women with anorexia nervosa. J Clin Exp Neuropsychol 2007;29(7):734-41.
[36] Stein D, Meged S, Bar-Hanin T, Blank S, Elizur A, Weizman A. Partial eating disorders in a community sample of female adolescents. J Am Acad Child Adolesc Psychiatry 1997;36(8):1116-23.
[37] Garner DM. EDI2: Eating disorder inventory-2, professional manual. psychological assessment resources. Florida: Odessa.; 1991.
[38] Boles DB. Hemispheric differences in the judgment of number. Neuropsychologia 1986;24(4):511-9.
[39] Claes L, Vandereycken W, Luyten P, Soenens B, Pieters G, Vertommen H. Personality prototypes in eating disorders based on the big 5 model. J Personal Disord 2006;20(4):401-16.
[40] Karwautz A, Rabe-Hesketh S, Hu X, Zhao J, Sham P, Collier DA, et al. Individual-specific risk factors for anorexia nervosa: A pilot study using a discordant sister-pair design. Psychol Med 2001;31 (2):317-29.
[41] Holliday J, Tchanturia K, Landau S, Collier D, Treasure J. Is impaired set-shifting an endophenotype of anorexia nervosa? Am J Psychiatry 2005;162(12):2269-75.
[42] Benninghoven D, Tetsch N, Jantschek G. Patients with eating disorders and their siblings: An investigation of body image perceptions. Eur J Child Adolesc Psychiatry 2008;17(2):118-26.
[43] Steiger H, Stotland S, Trottier J, Ghadirian AM. Familial eating concerns and psychopathological traits: Causal implications of transgenerational effects. Int J Eat Disord 1996;19(2):147-57.
[44] Hay P, Fairburn C. The validity of the *DSM-IV* scheme for classifying bulimic eating disorders. Int J Eat Disord 1998;23(1):7-15.
[45] Van Hanswijck de Jonge P, VanFurth EF, Lacey JH, Waller G. The prevalence of *DSM-IV* personality pathology among individuals with bulimia nervosa, binge eating disorder and obesity. Psychol Med 2003; 33(7):1311-7.
[46] Fassino S, Amianto F, Abbate-Daga G. The dynamic relationship of parental personality traits with the personality and psychopathology traits of anorectic and bulimic daughters. Compr Psychiatry 2009;50 (3):232-9.
[47] Woodside DB, Bulik CM, Halmi KA, Fichter MM, Kaplan A, Berrettini WH, et al. Personality, perfectionism, and attitudes toward eating in parents of individuals with eating disorders. Int J Eat Disord 2002;31(3):290-9.
[48] Klump KL, Kaye WH, Strober M. The evolving genetic foundations of eating disorders. Psychiatr Clin North Am 2001; 24(2):215-25.
[49] Klump KL, Miller KB, Keel PK, McGue M, Iacono WG. Genetic and environmental influences on anorexia nervosa syndromes in a population-based twin sample. Psychol Med 2001;31(4):737-40.