Depression, anxiety and obsessive–compulsive symptoms in relation to nutritional status and outcome in severe anorexia nervosa

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A B S T R A C T

Depression, anxiety and obsessive–compulsive disorder are frequently reported to co-occur with anorexia nervosa (AN). There is clinical consensus that depressive symptoms and anxiety may in part be sequelae of malnutrition in AN. However, evidence-based data are still very rare. The present study among severe AN patients investigates links between these psychological variants and nutritional status at admission and subsequent to nutritional rehabilitation. Twenty-four women with AN diagnosed according to the Diagnostic and Statistical Manual IV (DSM-IV) were included prospectively and consecutively at hospitalisation. Nutritional status was assessed by body mass index (BMI). Several psychological aspects were assessed using various scales for depression, anxiety, social phobia, obsessive and eating behaviour symptoms. Follow-up weights and heights at 4–12 years after hospital discharge were measured in 18 patients. BMI and all the scores except the Yale-Brown obsessive–compulsive scale (Y-BOCS) showed significant improvement between admission and discharge. This study highlights the fact that some of the depressive and anxiety symptoms at least partially decrease with nutrition rehabilitation. The improvement in the scores on the psychometric scales between admission and discharge was not correlated with BMI improvement. Psychometric scores at admission and at discharge were not correlated with BMI at follow-up. BMI at follow-up was correlated with minimum lifetime BMI ($r=0.486$, $P=0.04$). Future studies should use a better indicator for nutritional status than BMI alone, and should also consider the initial degree of weight loss and the rate at which weight was lost.

1. Introduction

Depressive disorders, anxiety disorders and obsessive–compulsive disorder (OCD) are frequently reported to co-occur with anorexia nervosa (AN).

It has even been suggested that AN is essentially a form of depressive illness (Kay, 1953; Hendren, 1983) or OCD (Hudson et al., 1987; Altman and Shankman, 2009). On this point, the literature does not always differentiate between the ‘symptoms’ (depressive, anxiety or obsessive symptoms) and the ‘diagnoses’ (major depressive disorder, OCD or anxiety disorders). In AN, both co-morbidity with anxiety disorders, OCD and depressive disorders, and presence of symptoms of anxiety, obsession and depression are very frequent (Godart et al., 2002; Touchette et al., 2010).

Clinical consensus agrees that depressive ‘symptoms’ and anxiety are partially sequelae of malnutrition in AN (American Psychiatric, 2006). Despite the long-standing implication of malnutrition in causing anxiety and depressive symptoms (the Keys study in 1950 (Keys et al., 1950)), evidence-based data are still very rare (Mattar et al., 2010). The malnourished status of the patient is a fundamental clinical and somatic aspect of AN. However, questions can be raised as to whether the psychiatric symptoms are totally or partially the consequence of malnutrition and weight loss, or whether malnutrition is a variant of certain psychological factors (Pollice et al., 1997; Meehan et al., 2006). To our knowledge, seven studies have investigated the relationship between BMI or weight and depression/anxiety symptoms. All found a decrease in depression and anxiety symptoms (and frequently in eating behaviour symptoms) after treatment accompanied by an increase in weight gain, but they do not draw the same conclusions concerning the link between nutrition rehabilitation and the improvement in psychological condition. Some
Studies found evidence-based data in favour of (Eckert et al., 1982), or against (Channon and deSilva, 1985) a positive link between the course of nutrition rehabilitation and the attenuation of depressive and anxiety symptoms, while others only discussed this link but did not test it (Pollice et al., 1997; Meehan et al., 2006; Mattar et al., 2010).

None of these studies considered the link between the degree of weight loss due to AN, and the intensity of psychological symptoms. However, the greater the weight loss the greater is the biological impact. We therefore hypothesised that the greater the weight loss the more marked were depressive, anxiety and obsessive symptoms likely to be in patients with AN. Furthermore, among these previous studies, none investigated social phobia symptoms, although social phobia is one of the most frequent anxiety symptoms in women with eating disorders. The incidence is 3 to 10 times higher than in the general population (Kessler et al., 1994; Lilenfeld et al., 1998). None of the studies explored depression, anxiety, OCD and social phobia in conjunction in relation to malnutrition.

Finally, while the link between the severity of current eating disorder and the severity of depressive symptoms has been previously investigated (Herpertz-Dahlmann and Remschmidt, 1993), no study has followed patients to examine the link between the intensity of psychological symptoms and nutritional status at admission and in long-term outcome.

Consequently, the aim of the present study among AN patients was to investigate the links between (1) depressive, anxiety (including social phobia), obsessive and eating behaviour symptoms and the nutritional status at admission (current BMI and the scale of weight loss) and duration of illness, (2) the evolution of the above psychological symptoms and nutrition rehabilitation (the evolution of BMI gain) and (3) nutritional status and psychological symptoms at admission and discharge and in long-term outcome (in terms of BMI).

2. Methods

2.1. Subjects

Twenty-four Diagnostic and Statistical Manual IV (DSM-IV) restrictive sub-type AN females aged between 13 and 21 years were included prospectively and consecutively at admission to the psychiatry unit for adolescents at Institut Mutualiste Montsouris, Paris, France between 1999 and 2000. One of the main objectives of the inpatient programme is weight gain, and has been previously described (Godart et al., 2004; Godart et al., 2009). The patients were evaluated by a trained psychologist within 1 week of their admission (T0) and in the week prior to discharge (Tfinal). Later, 4–12 years after hospital discharge, follow-up weights and heights were measured in the course of a larger follow-up study (Hubert, 2010). In the follow-up, all patients were still alive but we only obtained information concerning 18 patients from the initial sample of 24 because six patients did not have proper data recorded in their charts. These studies (initial evaluation and follow-up) were approved by French ethics committees (the Comité consultatif de Protection des Personnes dans la Recherche Biomédicale (CCPPRB) and the Commission nationale de l'informatique et des libertés (CNIL)).

2.2. Assessments

The evaluation was performed using the following measures:

- Nutritional status: The body mass index (BMI) in kg m⁻² calculated as weight/(height)². Patient weight was measured in light clothing to the nearest 0.1 kg and height was measured to the nearest 0.1 cm. Patients were classified according to Cole's index of thinness (Cole's index is a set of three cut-offs to define thinness in children and adolescents, based on BMI at age 18 years, the 3rd class corresponding to BMI under 16 kg m⁻²). Patients were classified according to Cole's index of thinness (Cole's index is a set of three cut-offs to define thinness in children and adolescents, based on BMI at age 18 years, the 3rd class corresponding to BMI under 16 kg m⁻²). Patients were classified according to Cole's index of thinness (Cole's index is a set of three cut-offs to define thinness in children and adolescents, based on BMI at age 18 years, the 3rd class corresponding to BMI under 16 kg m⁻²).
- Degree of weight loss: Estimated as the difference between maximum lifetime BMI (self-reported height and weight) and BMI at admission (BMImin).
- Depressive symptoms: The Beck Depression Inventory (BDI) (Beck et al., 1961) and the Hamilton Rating Scale for Depression (HRSID) (Schwab et al., 1967). The BDI is a self-rating scale of 21 items that assesses cognitive and motivational symptoms of depression at the time of evaluation. The HRSID, a clinical interview comprising 17 items, assesses the severity of depressive symptoms (psychological and somatic) over the past 7 days in a straightforward, quantitative manner.
- Anxiety symptoms: The Spielberger State–Trait Anxiety Inventory (STAI-I, II) (Spielberger, Gorsuch and Lushene, 1970) and the Hamilton Rating Scale for Anxiety (HARS) (Hamilton, 1959). The HARS is a clinical interview of 17 items that assesses behavioural and somatic symptoms associated with anxiety in the past 7 days. The STAI is a widely used self-report instrument, gives separate scores for state and trait anxiety.
- Social phobia symptoms: The Liebowitz Social Anxiety Scale (LSAS) (Yao et al., 1999), a clinical interview divided into 2 sets of 25 questions each concerning current fear and avoidance in social interactions and performance-oriented situations.
- Obsessive–compulsive symptoms: The Yale-Brown Obsessive–Compulsive Scale (Y-BOCS) (Goodman et al., 1989), a semi-structured interview designed to rate the severity, the number and the type of symptoms for the previous week.
- Eating behaviour symptoms: The Yale-Brown Obsessive–Compulsive Scale for Eating Disorders (Y-BOCS-ED), which measures eating disorder-related preoccupations and rituals (Sunday et al., 1995).

2.3. Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) 17.0. Descriptive statistics were processed in a first step. Results are presented as means (S.D). Then, the relationships between the different scale scores and BMI, the duration of illness and the difference between maximum BMI and BMIfinal were tested using Spearman's correlations (sample < 30) at admission (T0) and at discharge (Tfinal). Evolutions were calculated using the differences in score or BMI between admission and discharge data for each variable (depressive, anxiety, obsessive–compulsive, social phobia and eating behaviour symptoms). Non-parametric paired tests (Wilcoxon signed-rank test) were performed to check the evolution of BMI and the evolution of each score between admission and discharge. Spearman correlations were performed to check for relationships between BMI changes and psychometric score changes. BMI at follow up was correlated with psychometric scores at admission and discharge, to detect any factor linked to follow-up nutritional status (BMI).

3. Results

3.1. Sample characteristics

The clinical characteristics of the 24 subjects are presented in Table 1. The mean age of the participants at admission was 16.4 years (1.9). The duration of the inpatient treatment was 3.2 (2.0) months on average. Mean BMI at admission was 13.8 kg m⁻² (1.3), and height was measured to the nearest 0.1 cm. Patients were classified according to Cole's index of thinness (Cole's index is a set of three cut-offs to define thinness in children and adolescents, based on BMI at age 18 years, the 3rd class corresponding to BMI under 16 kg m⁻²). All of the patients were under the 3rd class of thinness for their age using Cole's index of thinness. At discharge, mean BMI was 17.8 (1.2) and all patients had moved to a higher class of thinness for age (6 patients reached the 2nd class and 18 patients reached the normal class).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patients' (n=24) characteristics and the duration of treatment.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td><strong>Minimum</strong></td>
</tr>
<tr>
<td>Age (years)</td>
<td>16.38</td>
</tr>
<tr>
<td>BMIminit (kg/m²)</td>
<td>13.84</td>
</tr>
<tr>
<td>BMImfinal (kg/m²)</td>
<td>17.79</td>
</tr>
<tr>
<td>BMIfollow-up (kg/m²)</td>
<td>18.21</td>
</tr>
<tr>
<td>Minimum BMI during lifetime (kg/m²)</td>
<td>13.37</td>
</tr>
<tr>
<td>Maximum BMI during lifetime (kg/m²)</td>
<td>21.28</td>
</tr>
<tr>
<td>Duration of illness (year)</td>
<td>0.98</td>
</tr>
<tr>
<td>Duration of inpatient treatment (month)</td>
<td>3.20</td>
</tr>
<tr>
<td>Intensity of weight loss</td>
<td>7.44</td>
</tr>
</tbody>
</table>

BMI: Body Mass Index; BMIminit BMI at admission; BMImfinal BMI at discharge; BMIfollow-up BMI at follow-up; S.D: Standard Deviation.

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*, **a** all data concerns 24 patients during the inpatient treatment except BMIfollow-up concerning 18 patients at follow up.
The mean duration of follow-up after discharge was 7.1 years (2.4) with a median of 8.3 years. The mean BMI was 18.2 kg m\(^2\) (3.0). Six of the 18 patients followed up had improved but still met the AN criterion with BMI still below 17.5 kg m\(^2\) (threshold weight criterion for AN in adults), respectively 10.9; 16.8; 14.5; 16.0; 15.9; and 15.4 kg m\(^{-2}\).

Psychometric scores at admission and at discharge were not correlated to BMI at follow-up (Table 2).

BMI at follow-up was correlated with minimum lifetime BMI \(r=0.486, P=0.04\) and was independent from the duration of follow-up.

4. Discussion

Our study shows a significant attenuation in depression, anxiety, social phobia and eating behaviour symptoms in AN patients between hospital admission and discharge, along with an improvement in BMI. To our knowledge, our study is the first to consider depression, anxiety, OCD and social phobia in relation to malnutrition in the same study, to explore the link between the degree of weight loss (and not solely initial weight status) and the intensity of these psychological symptoms and to assess follow-up weights and heights over 4–7 years in the same patients.

Concerning depressive symptoms, our results are in line with the results of Pollice et al. (Pollice et al., 1997), who used the same scales and found a significant decrease in HDRS and BDI scores in relation to weight gain in 22 patients followed from underweight to short-term weight recovery, reaching over 90% average body weight (in 1 month on average). Similarly, Meehan et al. (Meehan et al., 2006), who focussed on the evolution of depressive symptoms and BMI, found improvement in scores on the BDI and improvement in weight gain from admission of their 21 patients until they reached 90% of their ideal body weight (IBW) (i.e., mean ± S.D.=19.9 ± 6.3). They concluded that the evolution of the level of depressive symptoms was linked to nutrition rehabilitation, but they did not test for a direct link between depressive symptoms and malnutrition (Mattar et al., 2010). We tested this link and did not find any link between the course of weight gain and the course of depressive symptoms. In the same way, in a 45-patient sample, Channon et al. (Channon and deSilva, 1985) did not find any relationship between the course of depression (Wakefield Depression Inventory) and changes in weight, although, as in our study, they found significant improvement in depression symptoms between admission and discharge (\(P<10^{-4}\)) and a significant improvement in weight.

We hypothesised that the greater the BMI loss the more likely are depressive symptoms to be present in patients with AN. However, we did not find any significant correlation with this BMI indicator and depressive symptoms at admission.

Concerning anxiety symptoms, scores on the scales assessing anxiety (HARS and STAI) significantly decreased between admission and discharge. However, at admission, we did not find the scores on the STAI state or trait or the HARS scores to be correlated with BMI, which is similar to the results by Kawai et al. (Kawai et al., 2008).

Previously, Pollice et al. (Pollice et al., 1997) only described the course of ‘anxiety’ symptoms in relation to short-term weight gain: their descriptive results showed that the most underweight patients (no BMI cited) had the highest scores for anxiety symptoms, as measured by the HARS but not the STAI-state. In fact, the HARS measures mainly the somatic symptoms of anxiety. These symptoms are very similar to physical symptoms that are associated with malnutrition; vitamin deficiencies, mineral

### Table 2

<table>
<thead>
<tr>
<th></th>
<th>Admission Mean (S.D)</th>
<th>Discharge Mean (S.D)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m(^2))</td>
<td>13.84 (1.26)</td>
<td>17.79 (1.21)</td>
<td>.000</td>
</tr>
<tr>
<td>BDI</td>
<td>9.79 (4.92)</td>
<td>3.21 (4.80)</td>
<td>.000</td>
</tr>
<tr>
<td>HDRS</td>
<td>14.56 (5.68)</td>
<td>2.0 (2.43)</td>
<td>.000</td>
</tr>
<tr>
<td>Liebowitz global score</td>
<td>47.04 (28.30)</td>
<td>24.95 (26.91)</td>
<td>.005</td>
</tr>
<tr>
<td>HARS</td>
<td>11.0 (6.55)</td>
<td>1.67 (1.76)</td>
<td>.000</td>
</tr>
<tr>
<td>HARS somatic anxiety symptoms</td>
<td>2.6 (2.88)</td>
<td>0.5 (0.65)</td>
<td>.01</td>
</tr>
<tr>
<td>HARS psychological anxiety symptoms</td>
<td>8.4 (4.39)</td>
<td>1.67 (1.60)</td>
<td>.000</td>
</tr>
<tr>
<td>STAI-trait</td>
<td>52.8 (9.20)</td>
<td>35.8 (12.01)</td>
<td>.000</td>
</tr>
<tr>
<td>STAI-state</td>
<td>46.1 (11.65)</td>
<td>32.1 (11.81)</td>
<td>.002</td>
</tr>
<tr>
<td>YBOCS</td>
<td>6.33 (9.12)</td>
<td>1.875 (5.79)</td>
<td>.051</td>
</tr>
<tr>
<td>YBOCS-ED</td>
<td>15.0 (5.65)</td>
<td>10.0 (5.66)</td>
<td>.027</td>
</tr>
</tbody>
</table>

Non-parametric analysis (Wilcoxon signed-rank test). \(p<.05\). S.D: standard deviation.


Seven of the 24 patients received anti-depressant treatment during hospitalisation. Statistical comparison (analysis of variance, ANOVA) on all psychological scores did not show any difference between patients on anti-depressant treatment and patients receiving no medication. We therefore considered all 24 patients together for the following analyses.

3.2. At admission

Admission BMI and the degree of weight loss were not correlated with psychometric scores at admission (Table 3). The duration of illness was correlated only with the Y-BOCS-ED admission score; the longer the illness, the more intense were ED symptoms \(r=0.547; P=0.01\).\(^{2}\)

3.3. At discharge

Discharge BMI was not correlated with the depressive, anxiety, social phobia or obsessive-compulsive scores at discharge (Table 3). It was positively correlated with the Y-BOCS-ED score at discharge \(r=0.886, P=0.019\) (Table 3).

3.4. Evolution between admission and discharge

Psychometric scores (for depressive, anxiety, social phobia and eating behaviour symptoms) showed significant decreases between \(T_{\text{initial}}\) and \(T_{\text{final}}\), except for obsessive-compulsive symptoms, where only a tendency was observed \(P=0.051\) (Table 2). During the same period, BMI increased significantly \(P<0.0001\). Improvement on the Liebowitz scale was also significant even when we removed the eating behaviour items \(P=0.006\).

3.5. Relationship between change in BMI and changes in the psychometric scores

The improvement in the ‘global’ scores on the psychometric scales between admission and discharge was not correlated to BMI improvement. Table 3 shows the correlations between changes in BMI and changes in each of the psychometric scale scores.

\(^{2}\) \(r\) is Spearman’s Rho.
depletion and decreased food intake can also cause cardiovascular, muscular, autonomic and many other physical symptoms (Gola et al., 1976, 2009; Forest et al., 2009; Taylor et al., 1948). This might lead to an artefact, and be a source of confusion in the aetiology of the symptoms and their improvement.

These results could be explained by the fact that BMI might not be an indicator that adequately reflects either malnutrition or improvement in nutritional status. In cases of severe malnutrition, BMI is not in fact a sensitive tool for determining nutritional status (Moreno et al., 2008; Trocki et al., 1998). The loss of body cell mass can be offset by extra-cellular fluid accumulation and thus cannot be accurately detected by body weight measurement (Kyle et al., 2004; Mattar et al., 2011). Moreover, constitutional variations between individuals affect BMI and make it less sensitive to detecting changes in nutritional status. This point highlights a problem encountered by the present study, and also many previous studies, the problem of an incomplete nutritional assessment (Mattar et al., 2010).

Our results show that the Y-BOCS scores between $T_{\text{initial}}$ and $T_{\text{final}}$ tend to decrease. If we compare our results to Pollice et al., they also found significant improvement in patients using the Y-BOCS in relation to stages in weight restoration (underweight to short-term weight recovered) (Pollice et al., 1997). Conversely, Channon et al., with a larger sample, found neither a significant correlation between the level of obsessive–compulsive symptoms measured by MOCI (Maudsley Obsessional–Compulsive Inventory) and weight gain (in kg, not BMI) (Channon and deSilva, 1985), nor a significant change between MOCI evaluation times independently from weight. However, the MOCI is a self-administered measure, and the Y-BOCS is a hetero-administered questionnaire; in addition, it does not measure the same obsessive–compulsive symptoms, but rather obsessive complaints; in clinical trials, the sensitivity of the MOCI to change has been found to be very poor (Goodman and Price, 1992).

Concerning social phobia, our results show that LSAS scores significantly decreased with inpatient treatment. Even when the eating behaviour items were removed from the global score, we did not find social phobia symptoms correlated to BMI evolution. The links between AN and social phobia are not widely documented. Nevertheless, social phobia occurs frequently in AN (Halmi et al., 1991; Casper, 1998) and to our knowledge, no work has examined the evolution of social phobia symptoms in addition to depressive and other anxiety symptoms in the course of improvement in nutritional status in AN.

It is still unclear what components of depression, anxiety (including social phobia) and obsessive–compulsive symptoms are linked to malnutrition and what component is prior to or concomitant with AN independently from malnutrition. In fact, Maeselle et al. (Maeselle, Stice and Hogansen, 2006) showed that in adolescent females initial depression predicted later increases in eating disorder symptoms. Further, Touchette et al. (Touchette et al., 2010) found that an atypically high anxiety trajectory in childhood increased the likelihood of developing eating disorder symptoms (i.e. sub-clinical binge eating disorder) at age 16 years by 1.7. Moreover, a follow-up study showed that female patients with AN had higher rates of depression than controls after a 10-year follow up period (Halmi et al., 1991). It has been previously demonstrated that the severity of depressive symptoms in AN is linked to the severity of the eating disorder (Herpertz-Dahlmann and Remschmidt, 1993). Our results on long-term outcome (evaluated by BMI at follow-up) did not relate BMI to psychological symptoms at admission to or discharge from inpatient treatment. However, it was related to minimum lifetime BMI, which is in line with previous findings (Steinhausen, 2002). Patients who reached the lowest lifetime BMI levels tended to have the lowest BMI at follow-up. Minimum lifetime BMI might therefore be a good indicator of the severity of AN.

4.1. Limitations

As stated previously, a core of the descriptive clinical literature supports the fact that malnutrition is implicated in causing anxiety and depressive symptoms (Keys et al., 1950). This relationship did not appear in our results, possibly as a result of three different factors: the degree of weight restoration (some patients only reached class 2 thinness for age on Cole’s index), the relatively short mean period of weight restoration and the small sample size. The sample size could have led to false negative results for the tests due to restricted power, especially concerning BMI. In addition, the patients had a global treatment programme during their hospitalisation, which aimed at restoring weight, altering anorexic attitudes, treating any medical complications, supporting and treating the family, enhancing autonomy, facilitating identity formation and increasing self-esteem by means of psychotherapy (Godart et al., 2004; Godart et al., 2009). This treatment had amounted to a possible confounder in the improvement of their depressive and anxiety symptoms. Indeed, the study did not assess nutritional rehabilitation in the absence of other interventions.

Furthermore, nutritional status requires a more complete assessment (not solely BMI) to be correctly defining stages in nutritional rehabilitation. The evaluation of the scale of weight loss from the difference between maximum BMI and BMI$_{\text{initial}}$, is approximate, as the course of AN in certain patients is not linear or continuous. Nevertheless, because the duration of illness in our study was not very long (1 year), this indicator could be quite acceptable and should be tested in future studies.
Another limitation is the lack of information about premorbid and co-morbid depression and anxiety or psychotropic drug use in the study population.

Finally, an adjustment on confounding variables was not possible on account of the small number of parameters available.

4.2. Conclusion

Our study support the fact that depression and anxiety symptoms at least partially improve with nutrition rehabilitation, and do not predict long-term outcome in terms of BMI. We failed to show a link between BMI and depressive/anxious symptoms and weight gain.

Future studies should use larger samples and a better indicator for nutritional status, for example, body composition and biological markers. They should also consider the scale of initial weight loss and the rate at which weight loss occurred to determine whether depression and anxiety symptoms are at least partially attributed to malnutrition in AN. Ideally, batteries of self-report questionnaires and interviews should be used for the psychological evaluations. As recommended previously (Garner, 1993), nutrition rehabilitation should be conducted before considering introducing pharmacological treatment for anxiety or depression, because a large proportion of these symptoms improve with weight gain. In addition, in future research, detecting the patients with depression/anxiety symptoms that are not related to malnutrition could enable early intervention for these disorders.

References


