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Review

Relationship between malnutrition and depression or anxiety in Anorexia Nervosa: A critical review of the literature

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ABSTRACT

Background: Depression, anxiety and obsessive–compulsive disorder (OCD) frequently co-occur with Anorexia Nervosa (AN). Clinical consensus admits that depressive *symptoms* and anxiety are the sequelae of malnutrition in AN. This review presents a critical assessment of the literature that looked into the link between depression/anxiety symptoms in relation to malnutrition and their improvement throughout the treatment.

Methods: We performed a systematic search of literature in Medline and PsychInfo for all the studies done to investigate psychological factors in relation to malnutrition in AN using the keywords “Anorexia Nervosa”, “depression”, “anxiety”, “obsessive–compulsive disorder” and “malnutrition”. Only articles published between 1980 and 2010 in English or French were reviewed. From the articles on AN and depression, anxiety, and/or OCD, only the ones which investigated on the relation with malnutrition were kept. This search was complemented by a manual search. We also checked the reference lists of the articles we found.

Results: Seven papers were analyzed and critically reviewed for their methods and results. Results are contradictory and inconsistent at all levels of assessment.

Conclusions: Evidence based data is very rare. From the 7 reviewed studies, none of them draw the same conclusion. This is mainly due to the large differences in the samples' populations and the studies' protocols. Future studies are needed to focus on the relationship between depression/anxiety symptoms and malnutrition. A more critical nutritional assessment should be undertaken with multiple psychological assessment scales.

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1. Introduction

Depression, anxiety and obsessive–compulsive disorder (OCD) frequently co-occur with Anorexia Nervosa (AN) (Casper, 1998; Godart et al., 2002, 2007). It has been even said that AN is essentially a form of depressive illness (Kay, 1953; Hendren, 1983) or OCD (Altman and Shankman, 2009). Depression and anxiety also occur frequently in families of patients suffering from AN (Perdereau et al., 2008). At this point the literature does not always differentiate between the *symptomatology* (depressive or anxiety symptoms) and the *diagnoses* (major depressive disorder or anxiety disorders).

Indeed, the malnourished status of the patient is a fundamental clinical and somatic aspect of AN; however, questions have been raised about whether the psychiatric symptoms are totally or partially the consequence of malnutrition and weight loss, or whether eating disorders are variants of psychological factors (Pollice et al., 1997; Meehan et al., 2006). Clinical consensus admits that depressive *symptoms* and anxiety are the sequelae of malnutrition in AN (American Psychiatric, 2006). However evidence based data is very rare. Despite the long-time implication of malnutrition in causing anxiety and depressive symptoms—since Keys' study in 1950 (Keys et al., 1950)—very few studies have investigated on this aspect.

Consequently, the purpose of this paper is to conduct a critical literature review of studies that looked into the link between depression/anxiety symptoms in relation to malnutrition and their improvement throughout the treatment. In this article methodological issues of the studies will be discussed. Then their results will be presented and discussed.

2. Methods

We performed a systematic search of literature in Medline and PsychInfo for all the studies done to investigate psychological factors in relation to malnutrition in AN using the keywords “Anorexia Nervosa”, “depression”, “anxiety”, “obsessive–compulsive disorder” and “malnutrition”. From the articles on AN and depression, anxiety, and/or OCD, only the ones who investigated on the relation with malnutrition were kept. This search was complemented by a manual search. We also checked the reference lists of the articles we found. Only articles published between 1980 and 2010 in English or French were reviewed.

Nine studies were identified (Channon and deSilva, 1985; Coulon et al., 2009; Eckert et al., 1982; Kawai et al., 2008; Konrad et al., 2007; Pollice et al., 1997; Laessle et al., 1988; Wamboldt

et al., 1987; Meehan et al., 2006). However, two studies were excluded because they had many limitations (Konrad et al., 2007; Wamboldt et al., 1987). In the first study, the number of patients with AN was extremely small (9 patients) and results were reported case by case with no overall statistical analysis (Wamboldt et al., 1987). In the second study, 1) the criteria of diagnosis for AN were not mentioned 2) the sample size was very small (10 patients) and 3) and invalid methods for body composition measurements were used. We kept the study by Channon and deSilva (1985) although no clear diagnostic criteria were reported but we contacted the authors who clarified that they used the Russell and Hersov (1983) criteria. The seven included studies were published between 1982 and 2009 (Table 1 line 1). A meta-analysis could not be drawn due to the diversity of samples compositions, treatment approaches, criteria of diagnosis, the type of factors evaluated and the small number of papers. Therefore, the following is a descriptive review of methodological issues and findings.

3. Results

All articles included in this review are presented in Table 1.

First we compared the methods of the studies on six levels: criteria of diagnosis and inclusion, times of evaluations and types of studies, sample composition (size, subtypes, gender, age and duration of illness), types of treatment, nutritional/biological assessment tools and psychological assessment tools. We then presented the findings of the studies.

3.1. Methods

3.1.1. Criteria of diagnosis and inclusion

Diagnostic criteria were not the same for the 7 studies due to the different periods of study (from 1982 to 2009) (Table 1, line 3) (Association, 1987, 1994). The oldest study, by Eckert et al. (1982), used the Feighner diagnostic criteria (Feighner et al., 1972) which differs *mostly* from the DSM criteria in that a patient should not have any “other known psychiatric disorder, with particular reference to primary affective disorder, schizophrenia, obsessive–compulsive and phobic neurosis” (Finn, 1983). Thus in the study by Eckert et al. (1982) wide differences in the patients' initial recruitment and psychological state can be pointed out in comparison to the other studies. The study of Channon and deSilva (1985) did not mention using research criteria in order to diagnose AN however they clarified to us that they used the Russell and Hersov (1983) criteria.

Table 1

Methods of studies investigating psychological factors in relation to malnutrition in Anorexia Nervosa* (lines 1 to 13).

1	Reference	Eckert et al. (1982) (14)	Channon and Desilva (1985) (12)	Laessle et al. (1988) (17)	Pollice et al. (1997) (8)	Meehan et al., 2006 (9)	Kawai et al., 2008 (15)	Coulon et al., 2009 (13)	
2	Country	USA	United Kingdom	Switzerland	USA	USA	Japan	France	
3	Diagnosis criteria AN	Feighner criteria (22)	Russell criteria (19)	DSM-III (21)	DSM-III (21)	DSM-IV (20)	DSM-IV (20)	DSM-IV (20)	
4	Inclusion criteria	Admission	Consecutive in patient admission	x	x	x	X	x	
5	Time of evaluations	–Admission –35 days after hospitalization	–Admission –Discharge 1 year FU	–1 week after admission –FU after inpatient (mean duration 14.1 ± 3.1 months)	–1 month after admission	–After inpatient treatment: for the group 1	–Admission –80% IBW –90% IBW	–1 month prior to hospitalization –Admission	Sample 1: –Admission –Discharge Sample 2: –FU at months 0, 6, 12 and 18.
6	Data analysis type	Longitudinal	Longitudinal	Cross sectional	Longitudinal cross sectional case controlled study	Longitudinal	Cross sectional	Longitudinal	
7	ED Controls	105 x	45 x	64 x	48 18	21 x	24 x	24 (sample 1) 60 (sample 2)	
8	Gender	Women	42 women 3 men	Women	Women	Women	Women	Women	
9	Groups	x	x	Admission: 28 –14 AN –14 BN FU: 36 –28 AN –8 BN	–Group 1: 22 underweight AN and after short-term weight restored –Group 2: 26 after long-term weight restoration –Group 3: 18 controls	x	x	x	
10	AN type	x	x	x	–Group 1: 22 13 restrictor 9 binge/purge –Group 2: 26 13 restrictor 13 binge/purge	–14 AN binge-purge –7 AN restrictors	–12 restrictive –12 binge/purging	–Sample 1: 100% restrictive –Sample 2: 86.6% restrictive	
11	Age (years) Mean ± SD (range)	x	21 ± 6 (14–45)	–Admission: 21.2 ± 2.9 –FU: 22.0 ± 3.2	–Group 1: 18 ± 5 –Group 2: 24 ± 4 –Group 3: 23 ± 4	24.76 ± 5.8 (18–45)	23.9 ± 8.7	–Sample 1: 16 ± 2.04 (13–20) –Sample 2: 16.6 ± 1.6 (13–20)	
12	Duration of illness (years) Mean ± SD, (range)	x	3.6 ± 6.9 (0–11)	–Admission: 4.6 ± 4 –FU: 5.2 ± 2.3	–Group 1: 3 ± 4 –Group 3: 9 ± 4	8.62 ± 5.66	5.1 ± 5.6	–Sample 1: x –Sample 2: ≤ 3	
13	Type of inpatient treatment	Hospital programme with a behavioural modification programme duration = 14.1 months ± 3.1)	Hospital programme for AN (at least 1 month) Inpatient programme specialized in treatment of AN	Hospital programme (FU sample: treatment mean Inpatient research unit: structured behavioural treatment program aimed at normalizing eating behaviour and weight. No drug used.	Hospitalization program with CBT designed to restore weight and correct unhealthy concepts on body weight and shape. 3 of 24 on SSRI or SNRI.	–Sample 1: hospitalization –Sample 2: post-hospitalization FU			

AN: Anorexia Nervosa, BN: Bulimia Nervosa, ED: Eating Disorders, FU: follow up, x: no information.

* Emphasis on AN, table does not mention BN results.

Concerning the criteria for inclusion, only two studies clearly stated any (Channon and deSilva, 1985; Eckert et al., 1982) (Table 1 line 4). As a result, questions can be raised about the way patients were included (i.e. chosen or consecutive admissions). Furthermore, the 7 studies were conducted on hospitalized patients. This is probably due to the fact that the most severely malnourished patients are usually hospitalized and that it is easier to conduct studies in inpatient facilities. The drop out was never mentioned except in Meehan et al. (2006) (10 dropout/31) although it can affect the recruitment of subjects.

3.1.2. Times of evaluations and types of studies

The 7 studies are a mix of cross sectional and longitudinal designs (Table 1 line 6). Kawai et al. (2008) and Laessle et al. (1988) are the 2 cross sectional studies (Table 1 lines 5–6). The 5 others are longitudinal studies and assessed the patients at admission and at the end of the treatment in order to follow the improvement; some assessed them also at a follow-up period (at 1, 6 or 12 months). However, even in longitudinal designs, cross sectional analysis at admission, discharge and/or follow up were performed.

3.1.3. Sample composition (size, subtypes, gender, age and duration of illness)

The 7 studies had widely varying sample sizes ranging from 21 to 105 patients (Table 1 line 7). Studies with small sample size may not have enough significance in order to adequately draw conclusion upon their results.

Patients also differed upon inclusion in the protocols in terms of age, type of AN (restrictive vs. binge-eating/purging type), duration of illness in years and weight (Table 1, lines 10–12, 14). Only one study had included boys (Channon and deSilva, 1985) (Table 1 line 8).

The means of age ranged between 16 ± 2.04 (mean \pm SD) and 24.76 ± 5.80 , with some studies including both adolescents and adults (14–45 year-old) (Channon and deSilva, 1985), others only adults (18–45 year-old) (Meehan et al., 2006), or only adolescents (13–20 year-old) (Coulon et al., 2009). One study did not report the age of the patients (Eckert et al., 1982). The duration of illness was not reported for the studies by Eckert et al. (1982) and Coulon et al. (2009) for the sample 1 and no precision for sample 2. For the others, duration varied between 3 ± 4 and 9 ± 4 years (Table 1 line 12). The chronicity of AN affects negatively the outcome: the severity of the disorder as well as the frequency of anxiety and depression are more potent with patients having a longer duration of illness (Zipfel et al., 2000). This factor is also limiting when comparing between patients of different studies.

3.1.4. Type of treatments

Patients included in the 7 studies' protocols were current or previously hospitalized patients. One of the important differences across studies is the type of treatment given to inpatients. However treatments modalities and duration varied widely between facilities. Three studies did not detail the treatment programme (Pollice et al., 1997; Laessle et al., 1988; Channon and deSilva, 1985). Others focused on behavioural therapy aiming to restore weight (Table 1 line 13). However, none reported how much weight should be

gained for discharge or the variation of BMI between admission and discharge. Only 2 reported if pharmacological agents were used.

3.1.5. Nutritional and biological assessment tools

The nutritional status of the patients was assessed in all 7 studies with very basic tools: weight, variation in weight gain, BMI or percentage of ideal body weight (IBW) (Table 2 line 14). None of the articles that had adolescents in their sample population considered the BMI percentiles for age: the age of the patients affects the BMI values: average BMI increases with age in the general population (Rolland-Cachera et al., 1991).

Two studies have also focused on biological factors with the aim of investigating their relationship with depression (Table 2 line 15) (Laessle et al., 1988; Kawai et al., 2008).

3.1.6. Psychological assessments tools

Among the 7 studies, 6 assessed depression (Table 2 line 16), 4 investigated at least one type of anxiety symptom and 5 assessed at least one other psychological aspect (eating symptoms or personality traits or others, Table 2 line 18). Concerning depressive symptoms, 3 out of the 6 studies used the Beck Depression Inventory (BDI), a self-reported scale (Laessle et al., 1988; Meehan et al., 2006; Pollice et al., 1997). Others used different scales, and 2 of them (Pollice et al., 1997; Eckert et al., 1982) used self-reported questionnaires along with a clinical interview such as the Hamilton Rating Scale for Depression (HRSD) (Table 2 line 16).

Four studies investigated anxiety symptoms (Channon and deSilva, 1985; Coulon et al., 2009; Kawai et al., 2008; Pollice et al., 1997). Six different scales were used (Table 2 line 17) and thus different aspects and types of anxiety were assessed. Similarly, four studies assessed the eating symptoms of patients (Channon and deSilva, 1985; Coulon et al., 2009; Kawai et al., 2008; Laessle et al., 1988): the Eating Disorder Inventory (EDI) and/or the EAT-40 were used (Table 2 line 18).

3.2. Findings

The seven studies have a common main objective: to determine and investigate the relationship between psychological variants and weight in AN (cross sectional weight or longitudinal weight restoration). Depending on the measured parameters, assessment scales, statistical analysis, and sample characteristics, each study differs extensively from the others in terms of findings (Table 2 line 19). Thus, a comparison was not clear-cut.

3.2.1. Cross sectional findings

Some studies examine somatic or psychological factors in relation to BMI or weight at different specific times, such as on admission to the hospital when patients are the most severely malnourished or at discharge when usually they have at least partially normalised their weight, or at follow up (variant period). Results of studies are partially affected by the times of evaluation, and which make them inconsistent and contradictory.

Table 2Assessment tools and results of studies investigating psychological factors in relation to malnutrition in Anorexia Nervosa^a (lines 14 to 19).

1	Reference	Eckert et al. (1982) (14)	Channon and Desilva (1985) (12)	Laessle et al. (1988) (17)	Pollice et al. (1997) (8)	Meehan et al. (2006) (9)	Kawai et al. (2008) (15)	Coulon et al. (2009) (13)
14	Nutritional assessment tools	Δ weight	Weight for height Patient's desired weight	Weight	% IBW	BMI	BMI Food intake	BMI
	At admission	x	38.2 ± 5.34 kg	71.8 ± 6.7%	–Group 1 [*] : 72 ± 6%	14.38 ± 1.47	3.8 ± 1.6	–Sample 1 [*] : 13,8
	At discharge	x	52.4 ± 6.32 kg	x	–Group 2 [*] : 94 ± 3% [*]			–Sample 2 [*] : 16,9
	At FU	x	45.5 ± 9.97 kg	84.7 ± 11.5	–Group 3 [*] : 98 ± 9%			
15	Biological assessment	x	x	BHBA T3 cortisol	x	X	Glucose Insulin Cortisol Leptin Acylated and desacyl ghrelin SDS ¹	x
16	Depression assessment scales	The Raskin Mood Scale ¹ The HSCL ¹	WDI ¹	DS and BDI ¹	HRSD ² BDI ¹	BDI ¹		x
17	Anxiety assessment scales type (instrument)	x	Obsessionality (MOCI) ¹	x	Anxiety (HARS) ² (STAI I and II) ¹ Obsessionality (Y-BOCS) ²	x	Anxiety (STAI I and II) ¹	Social phobia (MINI) ² (Leibowitz) ²
18	Other assessment scales	The MMPI personality characteristic	EAT-40 ¹	EDI ¹	Y-BOCS-ED ²	x	VAS ¹ EDI ¹	GOAS ² Sample 2: EDI ¹ Y-BOCS-ED ²
19	Results: association between nutritional status, depression and/or anxiety	<i>Longitudinal</i> Weight gain negatively associated with depressive symptoms (the Raskin Mood Scale and the HSCL).	<i>Longitudinal</i> Weight gain not associated with depressive symptoms (WDI). Weight gain not associated with OCD symptoms (MOCI).	<i>Cross sectional</i> Body weight associated with depressive symptoms measured by the DS scores but not with BDI scores.	<i>Cross sectional and longitudinal**</i> Underweight patients had the highest: Depressive scores (BDI and HRSD). Anxiety scores (HARS and STAI-I). OCD scores (YBOCS).	<i>Longitudinal**</i> Improvement in the depressive symptoms (BDI) in patients reaching 90% of IBW.	<i>Cross sectional</i> BMI not associated with depression (SDS). BMI not associated with anxiety (STAI-I and II).	<i>Longitudinal</i> BMI not associated with social phobia.

AN: Anorexia Nervosa, BDI: Beck Depression Inventory, BHBA: beta-hydroxybutyric acid, BIA: Bioelectrical Impedance Analysis, BMI: Body Mass Index, BN: Bulimia Nervosa, BSI: Brief Symptoms Inventory, DS: Depression Scale (Von Zerssen's), ED: eating disorders, EDI: Eating Disorder Inventory, EAT-40: Eating Attitude Test, FU: follow up, GOAS: Morgan and Russell global assessment scale; HARS: Hamilton Anxiety Rating Scale, HRSD: Hamilton Rating Scale for Depression, HSCL: the Hopkins symptom Checklist, IBW: Ideal Body Weight, MAC: Mizes Anorectic Cognitions Scale, MMPI: the Minnesota Multiphasic Personality Inventory, MOCI: Maudsley Obsessional–Compulsive Inventory, N: number of patients, RMR: Resting Metabolic Rate, SCL-90: Symptoms Checklist 90R, SD: Standard Deviation, SDS: Zung Self-rating Depression Scale, STAI: Spielberg State-Trait Anxiety Inventory, VAS: Visual Analog Scale, WDI: Wakefield Depression Inventory, Y-BOCS-ED: Yale–Brown Obsessive–Compulsive Scale Yale–Brown Eating Disorders. x: no information, Δ: change.

^a Emphasis on AN, table does not mention BN results.

¹ Self-rating scale.

² clinical Interview.

* At admission.

** No statistic testing of the relationship between BMI and depression/anxiety scale.

3.2.1.1. Depression. Among 3 studies concerning depression, only 2 (Laessle et al., 1988; Kawai et al., 2008) studied the direct link between depressive symptoms and the BMI (with contradictory results). The third study compared 3 groups of patients at 3 different levels of nutritional status (Table 2 line 14) (Pollice et al., 1997).

In Laessle et al. (1988) the authors clearly differentiate between specific depressive symptoms and the global depressive syndrome. They have found that depressive symptoms (measured by the Depression Scale (DS) and not by the BDI) such as mood disturbance may be associated with the body weight and biological parameters of starvation (beta-hydroxybutyric acid) and not with the time of evaluation (admission, discharge and follow up). On the contrary, in the study by Kawai et al. (2008), the BMI at one day after admission was not found correlated to depression symptoms (Zung Self-rating Depression Scale).

Pollice et al. (1997) found the intensity of depressive symptoms (measured by the BDI and the HRSD) to be most severe in the underweight patients (before the treatment) ($p < 10^{-5}$). However, they did not test the direct link between BMI and depressive symptoms.

3.2.1.2. Anxiety. Only 2 studies investigated on this point and had contradictory findings. In the study by Pollice et al. (1997), anxiety (HARS and STAI-I, II) was most severe in the underweight patients (before the treatment) ($p < 10^{-5}$). Similarly to depression, they did not study the direct link between anxiety symptoms and BMI.

Once again, with a small sample, Kawai et al. (2008) did not find that the BMI is correlated to anxiety (STAI-I and II) at one day after admission.

3.2.1.3. Obsessions/compulsions. One study, by Pollice et al. (1997), tested obsessiveness (Y-BOCS) and found it to be most severe in the underweight patients, without testing the direct relation with BMI.

3.2.1.4. Symptoms of social phobia. Coulon et al. (2009) did not find, at admission or discharge, the score of the social phobia scale (Leibowitz Social Anxiety scale) to be correlated with the BMI ($p = 0.05$, $r = 0.4$) (Coulon et al., 2009).

3.2.2. Longitudinal findings

In the same line as cross-sectional findings, we found very few studies that investigated longitudinally on the relationship between psychological variants (mainly depression and anxiety) in relation to weight gain during treatment. Thus, this comparison becomes strictly limited.

3.2.2.1. Depression. Four studies out of 7 examined the relationship between evolution of depressive symptoms and malnutrition. Two (Eckert et al., 1982; Channon and deSilva, 1985) out of the 4 tested the direct link and the other 2 (Pollice et al., 1997; Meehan et al., 2006) only described the evolution of depressive symptoms without correlating it to the progression of the BMI, but inferred a possible link with nutritional status improvement.

Eckert et al. (1982) made the correlation between weight gain (without indicating how much weight was gained) and depression ratings and found a negatively significant correlation for all scales (the Raskin Mood Scale and the HSCL): the

more the patient gained weight the less depressed he/she was.

Channon and deSilva (1985) did not find any significance between the course of depression (Wakefield Depression Inventory) and changes in weight (and not BMI), although they found significant improvement in depressive symptoms scores between admission and discharge ($p < 10^{-4}$) and similarly, a significant improvement in weight.

As they did not study the direct link between depressive symptoms and malnutrition, Pollice et al. (1997), only found a significant decrease in the HDRS and the BDI scores with weight gain in the 22 patients followed from underweight to short-term weight recovered.

Similarly, Meehan et al. (2006) focused on the evolution of depressive symptoms and BMI: they found improvement in the scores of the BDI and improvement in weight gain from patients' admission till they reach 90% of their IBW, but did not correlate them together.

3.2.2.2. Anxiety. Only Pollice et al. (1997) investigated on the anxiety symptoms in relation to weight gain: their results show a significant correlation between anxiety symptoms measured by the HARS and the STAI-II in relation with stages of weight restoration (underweight to short-term weight recovered) but not with the STAI-I. Note that the STAI-I evaluate the anxiety state in the person and STAI-II evaluates the anxiety traits (disposition) (Spielberger, 1983).

3.2.2.3. Obsessions compulsions. Only two studies focused on obsessive symptoms in relation to weight gain (Pollice et al., 1997; Channon and deSilva, 1985), once again with different method of analysis and yielding contradictory results. Pollice et al. found significant improvement in patients using the Y-BOCS in relation to stages of weight restoration (underweight to short-term weight recovered) (Pollice et al., 1997). Conversely, Channon and deSilva with a smaller sample, found neither a significant correlation between the MOCI (Maudsley Obsessional-Compulsive Inventory) and weight gain (in kg, not BMI) (Channon and deSilva, 1985), nor a significant change between the times of evaluations for the MOCI independently from weight. However the MOCI does not diagnose OCD, but rather obsession complaints; in clinical trials, the sensitivity of the MOCI to change has been found to be very weak (Goodman and Price, 1992).

3.2.2.4. Symptoms of social phobia. In the study of Coulon et al. (2009) authors investigated on social phobia symptoms evolution but did not find it correlated to BMI evolution ($p = 0.09$, $r = -0.35$).

4. Discussion

Clinical consensus admits that depressive symptoms and anxiety are the sequelae of malnutrition in Anorexia Nervosa (American Psychiatric, 2006). However, evidence based data is very rare. Very few studies have investigated the course of depression and anxiety symptoms in relation to nutritional status and their improvement throughout the treatment. The comparison of those studies is complicated: the methodological issues presented in the first part of the results may

explain the lack of consistent findings. No single characteristic is homogenous for the seven studies.

For both cross-sectional and longitudinal findings, a considerable factor in the inconsistency of the results is the varying times of evaluations. Also the number and the composition of the sample populations play an important role (view “methods” section). For example, in the study by Laessle et al. (1988) AN and BN were pooled together. Moreover, studies having less than 30 patients might not carry enough power to draw conclusions from their results (i.e. studies by Kawai et al. and Meehan et al.) yet they instigate new perspectives for research. Besides, the initial nutritional status of patients is very diverse between different studies, which place the patients at various stages of depressive symptomatology and anxiety since the start of the protocol.

The scales used for psychological assessment differed widely among the 7 studies. Some are self-reported questionnaires and others are in the form of a clinical interview. Discrepancies between the two types of questionnaires have always been highlighted (Fairburn and Beglin, 1994). The denial, frequent in AN (Lock and Fitzpatrick, 2009) is probably more evident in an interview. Also patients might tend to underestimate the gravity of their physical and psychological state in a self-reported questionnaire.

Furthermore, for assessing depression, not only were the scales diverse among the studies, but also the cut-off scores used were not always reported. The BDI was frequently used: for example Meehan et al. (Meehan et al., 2006) used a score of 13 and above to be indicative of depression, while in 1994, Kennedy et al. questioned the predictive power of the BDI in AN and proposed that a score of 26 produced optimal results in terms of specificity and sensitivity (Kennedy et al., 1994). At this point, different interpretations of the psychological status of the patients are highlighted.

In the same line, comparison between the anxiety symptoms at a cross sectional level in relation to malnutrition might be biased because of the use of different scales measuring different forms of anxiety. Some methods focus on general anxiety symptoms (i.e. STAI and HARS) and others on specific symptoms (i.e. social phobia and MOCI).

For longitudinal findings, besides the discrepancies in the methods and the sample composition, the treatment modalities and durations altered the results. 1) The different target weights to be achieved require different duration of treatments; patients who spend more time in the hospital could benefit more on the somatic and psychological levels and thus cannot be compared to patients who had shorter duration of treatment. Only Eckert et al. (1982) had a fixed time of treatment (35 days). Furthermore, the most severe cases (clinically admitted to have the worst outcome (Strober et al., 1997; Baran et al., 1995)) tend to drop out more from inpatient program and thus patients finishing the treatment could be less serious cases.

Concerning duration of illness, patients with a longer duration of illness at the start of the research protocol might be more “resistant” to treatment and might not improve in the same manner. For example, in the study of Channon and deSilva some of the patients had duration of illness of less than a year compared to 9 years in Pollice et al. (Channon and deSilva, 1985; Pollice et al., 1997). The chronicity of the illness itself can induce depressive symptoms as in every chronic disease (de Groot et al., 2001; Gettings, 2010).

In the 7 studies, the range in weight, BMI or %IBW on admission suggests varying clinical severity of patients included, with the most severely affected patients having the lowest BMI (Hebebrand et al., 1996). There was high variability at inclusion and a comparison is not evident. At this point, we raised a key question about the nutritional assessment methodology for the seven studies. Each protocol had used an incomplete method and none of them tried to assess the nutritional status more “completely” (e.g. by determining body composition): In cases of severe malnutrition, body weight and/or BMI are not sensitive tools to determine the nutritional status (Moreno et al., 2008; Trocki et al., 1998). The loss of body cell mass can be compensated by extracellular fluid accumulation and thus cannot be accurately sensed by body weight measurement or by the BMI (Kyle et al., 2004). This fact raises questions about the accuracy in the nutritional evaluation and therefore the potential nutritional follow up. Furthermore, when dealing with children or adolescents, the age of the patient should be imperatively taken into consideration with the nutritional evaluation, which was not the case for the 3 papers that included adolescents (Table 1 line 11): BMI should be used with caution as it is relative to the age; i.e. a BMI of 17.5 would be on the 3rd percentile for a 19-year old but on the 50th percentile for an 11-year old (Golden et al., 2008). Complementary to body weight measurements, assessing the body's muscle and fat stores is fundamental for the diagnosis and treatment of malnutrition as well as for assessing the patient's nutritional status because AN has such a deep impact on body composition. Also, biological markers help in assessing the nutritional status in anorexic patients and in evaluating the efficacy of the recovery. Thus, future research needs to examine further the nutritional status as it tells us better on the patient's somatic state.

5. Conclusion

Malnutrition and depressive anxiety symptoms are usually described to be closely related in AN, but evidence based data remain rare. From the 7 reviewed studies, none of them draw the same conclusion. This is mainly due to the large differences in the samples' populations and the studies' protocols. Future studies are needed to study this relationship and clarify their contradictory results. In order to correctly examine those links, larger samples are needed and more nutritional assessment tools should be taken into consideration. The nutritional status deserves to be intensely assessed, and not to be limited only to body weight or BMI. In addition, both anxiety (general and specific) and depression symptoms should be evaluated on the same sample and they are closely related. Ideally, sets of self-reported questionnaires and interviews should be used for the psychological evaluations.

Finally, depression and anxiety should be assessed as symptoms and disorders in order to confirm that depression disorders and anxiety disorders are over diagnosed among malnourished patients, as has been clinically admitted but very rarely investigated.

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Conflict of interest

All authors of the present review article declare that they have no conflicts of interest or any other personal end.

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