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Eating Disorders and Gastrointestinal Diseases: relationship, coexistence and state of the art

Perturbações do Comportamento Alimentar e Doenças Gastrointestinais: relação, coexistência e estado da arte

Bárbara Alexandra Gonçalves Gomes Ferreira

ORIENTADO POR: Dra. Ana Raquel Malheiro Silva Oliveira
COORIENTADO POR: Mestre Helena Barbosa Trigueiro da Rocha

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Abstract

The most common ED are AN, BN and BED. Eating disorder patients often have both upper and lower gastrointestinal symptoms. Also, individuals with GI disorders can develop disturbed eating behaviours that can progress to ED.

This review aims to highlight the state of the art on the relationship of gastrointestinal comorbidities with anorexia nervosa, bulimia nervosa and binge eating disorder, as well as suggestions on the treatment of this occurrence.

The presence of disturbed eating behaviours is greater in patients with gastrointestinal disorders than in patients with healthy controls, but the direction of the relationship is not clear. Several studies were included, and it was found that approximately 98% of patients with ED meet the Rome II criteria for at least one functional gastrointestinal disease (FGID), with IBS being the most frequent. Chronic constipation is one of the most frequent symptoms in AN and BN, and diarrhea is a problem more associated with BED. Gastric emptying rate also seems to be decreased in AN and BN. This review also includes a reflection about the microbiota in ED patients.

This review reflects the importance of the comorbidity of eating disorders and gastrointestinal diseases as well as highlighting the need for more articulation between academic literature and clinical guidelines. Also, aim to shine a light on how a better understanding of this concomitance can assist the management of GI alterations in patients with ED, invoking more evidence in this area.

Keywords: Eating Disorders; Gastrointestinal Diseases; Coexistence; Review

Resumo

As PCA mais comuns são a AN, a BN e o TCAP. Os pacientes com perturbações do comportamento alimentar apresentam muitas vezes sintomas gastrointestinais superiores e inferiores. Também individuos com doenças GI podem desenvolver comportamentos alimentares perturbados que podem evoluir para PCA.

Esta revisão tem como objetivo destacar o estado da arte sobre a relação das comorbidades gastrointestinais com anorexia nervosa, bulimia nervosa e transtorno da compulsão alimentar periódica, bem como sugestões sobre o tratamento dessa ocorrência.

A presença de comportamentos alimentares perturbados é maior em populações com distúrbios gastrointestinais do que em populações com controlos saudáveis, mas a direção da relação não é clara. Vários estudos foram incluídos e verificou-se que cerca de 98% dos pacientes com PCA preencheram os critérios de Roma II para pelo menos uma doença gastrointestinal funcional (DGIF), sendo o SII a mais frequente. A obstipação crónica é um dos sintomas funcionais mais frequentes na AN e BN, e a diarreia um problema mais associado ao TCAP. A taxa de esvaziamento gástrico também parece estar diminuida na AN e BN. Nesta revisão também se encontra uma reflexão sobre o conteúdo do microbioma em indivíduos com PCA.

Esta revisão reflete a importância da comorbidade de PCA e doenças GI, bem como destaca a necessidade de maior articulação entre a literatura académica e as diretrizes clínicas. Além disso, visa esclarecer como uma melhor compreensão dessa concomitância pode auxiliar no controlo de alterações gastrointestinais em pacientes com PCA, invocando mais evidência nesta área.

Palavras-Chave: Perturbação do comportamento alimentar; doenças gastrointestinais; coexistência; revisão

List of abbreviations

AN- Anorexia Nervosa

BED- Binge Eating Disorder

BN- Bulimia Nervosa

CD- Coeliac disease

ED- Eating Disorder(s)

FD- Functional Dyspepsia

FGID- Functional Gastrointestinal Disorder

GI- Gastrointestinal

IBD- Inflammatory bowel disease

IBS- Irritable bowel syndrome

SCFAs- Short-chain fatty acids

Summary

1. Introduction

Disruptions to the gastrointestinal (GI) tract result in GI disorders including irritable bowel syndrome (IBS), coeliac disease (CD) and inflammatory bowel disease (IBD). With a worldwide prevalence of 11.2%[1] for IBS, 0.7% for CD[2] and about 1 in 209 adults suffer from some type of IBD[3]. Gastrointestinal diseases can all be managed via a life-long modification of the daily diet to avoid GI symptoms, these symptoms include nausea, bloating, constipation, diarrhea, changes in weight and abdominal pain[4]. Eating disorders (ED) are often associated with psychiatric and somatic comorbidities, among which GI complaints are especially frequent and greatly impact on the quality of life in these patients and may lead to serious, even life threatening, complications. Eating Disorders are very common, with 2–4% of the population meeting DSM-IV criteria for a full syndrome ED[5] this diseases are associated with significant functional impairment and numerous serious psychological problems.

There is usually a significant overlap between GI symptoms and other underlying comorbid diseases, there are even some GI complications that are exclusively observed in diseases such as anorexia nervosa or bulimia nervosa[6]. All dietary-controlled GI disorders require some form of prescribed dietary restriction as part of their management. Food restriction is associated with altered eating patterns[7]. The prescribed dietary restraint in GI diseases may place these individuals at risk for abnormal eating patterns, which may result in the development of harmful thoughts and attitudes towards food and body weight, that may in turn, lead to inappropriate eating practices[8].

The exact mechanisms are not yet understood but it is known that gastrointestinal symptoms closely interact with dysfunctional eating behaviour[6], due to the continuous need of this individuals to follow a continued restrictive diet[9, 10], and therefore, contribute to the development or maintenance of eating disorders. On the other hand, also malnutrition due to disordered eating may lead to physiologic changes to the GI system[11] and consequently the increase of gastrointestinal symptoms. Moreover, gastrointestinal comorbidities greatly impact on the patients' wellbeing and increase the necessity for intensified treatment and/or hospitalization[6].

This review aims to highlight the state of the art of the concomitance of gastrointestinal diseases and the three most common eating disorders, as well as highlighting the need for more articulation between academic literature and clinical guidelines. I also aim to shine a light on how a better understanding of this concomitance can assist the management of GI alterations in patients with ED.

2. Methods

The research for this review was carried out in the *PubMed* database, as described in Appendix A, where the different topics, respective search terms, boolean operators, and number of studies found are presented.

Only studies published up to May 31, 2023, in which the concomitant presence of disease or gastrointestinal symptoms and disturbances in eating behavior or disturbed eating behavior were compared, were included. Older studies, studies carried out in animal or *in vitro* models , and studies written in languages other than English were excluded. The selected studies were exported to the *Endnote*

software, where duplicates and papers that did not meet the inclusion criteria described above were subsequently eliminated.

3. Eating Disorders

The classification "eating disorders" describes a group of mental illnesses that are manifested through disturbance to feeding behaviours and body weight regulation, with subsequent compromise across key physiological systems, including gastrointestinal functions. The fifth edition of the Diagnostic and Statistical manual from the American Psychiatric Association[12] recognizes three primary diagnoses within the eating disorder category: anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED)[13].

The etiology of eating disorders is multi-factorial, with genetic factors, neurobiological, environmental, and socio-cultural influences, as well as psychological traits, being pointed as crucial determinants. This is evident, for example, in research which shows that relatives of a person with an eating disorder are 7–12 times more likely to develop the illness themselves[14]. Eating disorders are frequent diseases with a biopsychosocial pathogenesis and often associated with psychiatric as well as somatic comorbidities. These psychiatric comorbidities encompass e.g. anxiety disorders and insomnia[15], while somatic complications include e.g. cardiac alterations[16], hormonal imbalances[17, 18] and gastrointestinal symptoms, such as diarrhea, obstipation and abdominal pain[19].

AN is one of the most diagnosed eating disorders and is defined by a restriction of energy intake leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. Patients

report an intense fear of gaining weight or getting fat, in which there is a disturbance in the way weight or body shape is perceived[12]. AN can be further subtyped into the restrictive type (where patients limit their food intake to reduce body weight) and the purging type characterized by methods to counteract food intake, e.g., by self-induced vomiting[20].

BN is expressed through regular binge eating episodes and subsequent use of compensatory methods such as self-induced vomiting or laxative abuse. Patients experience a subjective loss of control resulting in the consumption of a large amount of food, which by definition, occurs at least once a week for three months[12].

BED is characterized by subjective loss of control during the episode and the consumption of large amounts of food. In contrast to bulimia nervosa, patients do not regularly apply compensatory methods. According to the DSM 5, the binge eating episodes occur at least once a week over a period of three months[12]. BED is frequently associated with medical comorbidities, especially obesity and its complications such as Type II diabetes mellitus, hypertension, and dyslipidaemia[21].

4. Eating Disorders and Gastrointestinal Diseases

Comorbidities are common in eating disorders with gastrointestinal complications being especially frequent[6]. A study reported that out of all patients with eating disorders, 96% complained about postprandial fullness, 90% about abdominal distension and more than 50% about abdominal pain, early satiety, and nausea[22]. IBS is a functional GI disorder that is frequently associated with psychosocial impairment[23]. It is suggested that somatization, neuroticism, and state and trait

anxiety might be considered as predictors of specific Functional Gastrointestinal Disorders (FGIDs)[24].

It has been suggested that ED behaviour has a strong impact on the function of the GI tract. The disablement of the GI function such as disordered motility can bolster typical symptoms of ED such as loss of appetite, self-induced vomiting, dysphagia, constipation, and bloating[25, 26]. In addition, the malnutrition occurring in ED[27], producing metabolic myopathy, as well as electrolyte depletion, seems to dramatically influence the impairment in gastric motility, gastric emptying and intestinal transit[28]. The prevalence of disordered eating patterns ranged between 5.3-44.4% in those with GI disease[8]. The combined evidence indicates that the presence of ED may be greater in those with GI disease than the reported norms for healthy controls[8].

When food arrives to the GI tract a multiplicity of signals are released from the enteroendocrine cells of the GI wall[29-31]. This allows the gradual distension of the gastric wall to accommodate food gives rise through the stimulation of the mechano-sensitive vagal afferent fibers[32], to the perception of fullness; which plays a central role in controlling meal size[33]. Nutrients influence postprandial GI functions, such as GI motility and GI hormone release, with effects on appetite perceptions and consequent energy intake linking central perceptions with the GI function[34].

Dysregulations of these physiological processes can adversely affect eating behaviour or provoke GI symptoms, such as exaggerated postprandial fullness, nausea, and bloating[35, 36].

Evidence of the clinical alterations that were identified along the GI tract, more prevalent in the three primary ED, will be analysed, considering the role of the GI tract as an organic system associated with food intake and its regulation.

4.1.1 Esophagus

Esophageal FGIDs common in ED include globus and functional dysphagia[37, 38], with globus being characterised as the non-painful sensation of a lump or a foreign body in the throat[39]. Patients may describe tightness, itching, tickling, mucus accumulation, or choking. However, globus does not impede passage of food, and in most patients, the sensation generally improves with swallowing[39]. In contrast, dysphagia is a subjective sensation of difficulty swallowing that is, not just the sensation of something being in the throat, but that movement of food is impaired in the throat and esophagus. Both globus and dysphagia are frequently reported among patients with ED and may impede oral intake. In inpatients with ED, globus and functional dysphagia have been reported in up to 5% and 16%, respectively[40]. Patients with purging type AN, as well as BN, may have an increased risk of developing Barrett's esophagus and an increased risk of developing esophageal cancer [6].

On the other hand, the huge food intake during a binge episode seems to alter the lower esophageal sphincter's function, influencing the amount of gastric reflux that reaches the distal esophagus and leading to heartburn and regurgitation[41, 42]. The acid reflux could promote the onset of dysphagia in these patients[42].

A recent study demonstrated that the presence and severity of the three symptoms considered to be esophageal in origin (dysphagia, heartburn and

regurgitation), were significantly higher in restrictive and binge-eating/purging types of AN patients compared to healthy controls[43].

4.1.2 Stomach

Dyspepsia and nausea are some of the most encountered symptoms among patients with ED and may contribute to reduced intake[40], with post-meal discomfort being reported in over 90% of ED patients[44]. AN patients commonly complain of having a disordered gastric motility, especially when they are in a refeeding phase[45], reporting also notably more fullness and less hunger than healthy controls[46]. A study using ultrasound-based assessment of gastric emptying described greater antral distension in patients with anorexia nervosa (n=23) compared to healthy controls (n=25) which was associated with a prolonged gastric emptying time in AN [47]. Intriguingly, while 66% of patients with purging type (n=12) had the maximum gastric dilation at the end of the meal, patients with restrictive type (n=11) had a slower dilation[47].

Besides, recent studies reported that gastric emptying rate decreases with psychotropic drugs' intake (like amitriptyline or buspirone) which explains the decreased gastric emptying rate in patients who take these psychotropic drugs[48]. Ghrelin is known to increase appetite and subsequently body weight but also implicated in the stimulation of gastrointestinal motility[49]. However, since ghrelin levels are already greatly increased in patients with anorexia nervosa[50], a further elevation might not induce a robust additional effect, which should be further investigated in controlled clinical studies[6]. Postprandial suppression of ghrelin is reduced in BN but not in AN[51].

Patients with BN complained of postprandial fullness, epigastric pressure, and nausea as their most frequent and bothersome dyspeptic symptoms[44]. Patients with bulimia nervosa often suffer from delayed gastric emptying[6]. Geliebter et al.[52] reported a normal gastric emptying rate after the fixed meal, which is confirmed by normal CCK levels in BED patients, unlike that observed in BN patients. Thus, the specific pattern of eating behavior could play a role in the development of functional dyspepsia (FD) symptoms. Furthermore, increased gastric capacity has been associated with co-existing lower gastrointestinal symptom, since large amounts of food may cause colonic discomfort due to the increased osmotic load downstream[53].

A few case reports described gastric dilation in patients with binge eating disorder associated with symptoms such as abdominal pain, nausea and vomiting after a binge eating episode which may result in gastric perforation[54, 55] with the need of surgical intervention[56]. The reduction of intramural blood flow due to gastric dilation can lead to gastric necrosis[55].

4.1.3 Intestine

Common bowel-related symptoms in ED are constipation, abdominal pain, and bloating[38]. Constipation is the most common FGID among inpatients getting ED treatment[24], with functional bowel disorders reported in up to 98% of inpatients with ED[40]. These disorders are equally present in the outpatient setting, where studies have shown that FGID symptom severity—including constipation symptoms[57] and IBS symptoms[58]—was associated with greater ED pathology. Boyd et al. showed that 98% of ED patients, whom 44% AN patients, met Rome II criteria for at least one Functional Gastrointestinal Disorders (FGIDs) and the most

prevalent was IBS[59]. Chronic constipation is a frequent and inconvenient disorder negatively impacting social life and quality of life, with a higher prevalence among females[60, 61]. Similar to AN, constipation is the most frequent in BN patients[62].

In AN and BN, chronic constipation might be the result of abnormal colonic function due to poor or substandard intake of food and electrolytic alterations secondary to purging behavior, especially laxative abuse. The purging behavior could lead to several GI disorders: first, due to chronic watery diarrhea leading to dehydration and different electrolyte imbalances such as hypokalemia and metabolic acidosis with higher risk of fatal arrhythmias[63]; second, due to melanosis coli, defined as a benign darkening of colonic mucosa due to chronic abuse of a specific type of laxative, gradually resolvable with laxative withdrawal[64]. Furthermore, it should be considered that constipation may be caused by antidepressants, particularly tricyclic antidepressants[65, 66].

The repetitive intra-abdominal pressure in addition to constipation, pelvic floor weakness and over-exercise is considered the rationale for the relationship between BN and rectal prolapse[67, 68].

BED showed a high frequency of lower GI symptoms such as diarrhea and a feeling of anal blockage[69]. The underlying mechanisms of lower GI symptoms in BED patients have not been clearly elucidated yet. Probably, the large amount of food, rapidly delivered in the small bowel, stimulates the intestinal secretion due to the osmotic load and promotes colonic motility, resulting in greater delivery of stool to the distal colon, reducing stool consistency and leading to diarrhea and urgency[69]. The association between binge eating disorder and IBS was studied as

well in 6827 men and 8841 women that filled in a web-based questionnaire. Binge eating disorder has been associated with IBS in male as well as female patients, a finding remaining significant after adjustment for BMI and psychiatric as well as somatic comorbidities[70].

According to a cohort study, (n=17,979) patients with celiac disease are over 2 times more likely to develop AN[71]. Since symptoms of both diseases overlap, another study shows how the occurrence of one disease may hamper/delay the diagnosis of the other (n=664)[72].

The impairment of gut motility might be associated with an alteration of gut microbiota reported to be involved in the control of several gastrointestinal processes[73]. Despite the fact that microbial richness increased following weight regain, alterations in intestinal microbiota remained[74] which might be associated with persistent abdominal symptoms[6].

4.1.4 Gut-Brain axis disorders and Microbiota

Deviation in the gut microbiota has been revealed in GI and extra-GI disorders, leading researchers to investigate the role of microbiota in the pathogenesis of several diseases[62], in particular eating disorders. The gut–brain axis, connected via neural, hormonal, and immunological pathways, is a bi-directional communication system that is initially recognized for its role in regulating digestive function and food intake[75]. There is a high prevalence of co-morbidity between psychiatric and gastrointestinal symptoms, e.g., 40–60% of patients with functional gastrointestinal disorders experience psychiatric symptoms[76] and up to 50% of psychiatric patients are diagnosed with irritable bowel syndrome[77],

which clearly suggests broader implications of this axis on gastrointestinal and brain functions.

In AN, significant changes in the quality, quantity, and composition of gut microbiota were found during weight modification. Alpha diversity was lower during the phase of weight loss[78-81] ,resulting in a reduction of Firmicutes[82] and SCFAs[82-84] and the increase of Bacteroides. A re-established Firmicutes/Bacteroides (F/B) ratio and an increase of SCFAs levels were reported during renourishment and weight gain[85-87]. The levels of SCFAs represent the indirect measurement of the microbial composition and are influenced by dysbiosis[82, 83], especially in the AN-Restricted subgroup, compared to the control group[82].

Data on BN and BED are limited but point in the direction of low alpha diversity and increase Firmicutes and *Enterobacteriaceae*[88].

A healthy gut microbiota profile improves health and prevents several disorders. The importance of the diet in regulating the physiological balance between Firmicutes and Bacteroides is well known, showing how diets rich in fibers and biotic supplements can restore the normal commensal flora even in eating disorders.

Nutritional rehabilitation represents one of the essential focuses for ED, and the intake of macronutrients can significantly affect the composition of microbiota[89, 90] reducing dysbiosis[88].

Only when we identify core group(s) of bacteria or functional guilds that are potential causative agents, are we in the position of developing evidence-based

microbiome-targeted treatments, as well as modifying current treatments to improve efficacy, to eventually benefit patients with eating disorders[13].

5. Critical Analysis

This review points out some important factors that must be considered in the treatment of patients with gastrointestinal disorders. There is an indication that individuals with GI disorders may be at greater risk of developing eating disorders than the general population[8], indeed the prevalence of eating disorders in GI patients may be higher than healthy controls, being approximately 5.3-44.4% of GI patients have some type of eating disorder[8].

Medical conditions such as IBD, CD and IBS with predominantly gastrointestinal symptoms are usually treated through diet, which often includes the exclusion of certain foods for a certain period with subsequent reintroduction (in cases for instance, of IBD and IBS), this withdrawal of food creates changes in the usual eating pattern of individuals who often notice improvements in their GI symptoms after following the prescribed diet. The improvement of GI symptoms seems to prevent the subsequent reintroduction of food as is desirable in dietary treatment, and as a result a disturbance of eating behaviour may already be installed at this stage, which may progress to an eating disorder. However, also the regulatory and anatomical changes that develop as a direct result of the malnutrition inherent in eating disorders can generate these GI symptoms experienced by ED patients.

Some behaviours that may be considered disturbed may result from characteristics of the food environment that make it difficult to adhere to a prescribed diet, such as the unavailability of gluten-free foods. More research is needed to explore the

specific eating patterns associated with GI disease and how these patterns relate to external dietary restrictions[8].

The most frequently reported esophageal functional symptoms in patients with eating disorders are globus, and functional dysphagia. Esophageal pathologies, such as esophageal cancer and Barrett's esophagus, seem to be more associated with ED such as BN and purging type AN[6]. Research shows that BN and BED are associated to gastric reflux in the distal esophagus, which leads to the occurrence of symptoms such as heartburn and regurgitation[42, 69].

Dyspepsia and nausea are the most reported stomach related functional symptoms in patients with eating disorders[40], about 90% of these patients report feeling postprandial discomfort[44].

Chronic constipation is a functional intestinal complaint more frequent in AN and BN that may be associated with electrolyte imbalances that result from purging behaviours[63] it may also be caused by psychiatric treatment of these patients with tricyclic antidepressants[65, 66].

Patients with BN are at greater risk of rectal prolapse essentially due to the intra-abdominal pressure that occurs during purgative behaviours, in addition to constipation and weakened pelvic floor that can also evidence the risk[67, 68].

The most common complaints in BED patients are diarrhea and feeling of anal blockage[69], this type of eating disorder also has a strong association with IBS[70]. CD and AN are often associated and sometimes the overlapping of the symptoms of both can hinder/delay the diagnosis[72].

About 40-60% of patients with GI disorders present psychiatric symptoms[76] and about 50% of psychiatric patients are diagnosed with IBS[77], this highlights the importance of the two-way brain-gut communication system. The microbiota greatly influences the general health of individuals, and its regulation avoids several disorders. Regarding the regulation of the intestinal flora, it is desirable to increase Firmicutes/Bacteroidetes ratio as well as SCFAs levels[82], in order to avoid dysbiosis. However, to really be able to act beneficially in the microbiota of GI patients with and eating disorders cooccurrence further studies on this topic are needed.

This review reflects the importance of the comorbidity of eating disorders and gastrointestinal diseases, as it reflects on the etiology and complex nature of both types of diseases and calls for more evidence in this area, in addition to the clinical impact (guidelines, awareness, etc.). It is important to underline that several of the studies are old and the vast majority represent case reports and not observational studies or clinical trials. Therefore, larger and controlled studies are needed to better understand the impact and bidirectionality of these disorders.

7. Conclusions

Literature indicates that people with dietary-controlled GI disorders may be at increased risk for ED. This is likely to interact back with GI symptoms and psychological distress[8]. In fact, in the last years there has been and increase in our knowledge about the co-occurrence of these complications[6]. However, the limited research in this area is concerning.There is a need to fully examine the interaction between the two disorders, and its repercussions in treatment. These

findings would help to manage such cases effectively and improve physical health and well-being[8]. It existes growing interest in the role of intestinal microbiota in the pathogenesis of ED, its changes through refeeding practices, and in the modulation of intestinal microbiota using nutritional interventions or psychobiotic application as a co-adjuvant to ED standard therapy. Future studies are needed to add new knowledge in this field, possibly creating new synergies among a broad array of scientists and clinicians[62]. This will help to better address therapeutic issues in these difficult medical conditions, whith an often underlooked severety[62].

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Appendixes

Appendix A

Search terms used for the different topics addressed in this review and respective results

Theme	Search terms, boolean operators and filters	Serch results *(Results after exclusion of duplicates and studies that did not meet the inclusion criteria)*
Gastrointestinal diseases and Eating Disorders	"Eating disorders" AND "gastrointestinal diseases" (previous 5 years) + Filters: "Review" (previous 5 years) + Filters: "Systematic Review" (previous 5 years) +Filters: "Meta-Analysis" (previous 5 years)	N=29 N=14 N=3 N=1
Gut Microbiota	"Gut microbiota" AND "eating disorders" +Filters: "Systematic Review" (previous 5 years) "Gut microbiota" AND "eating disorders treatment" +Fiters: "Systematic Review" (previous 5 years)	N=1 N=1
Treatment and Management	"Management of disorders of gut-brain interaction" AND "Eating disorders"	N=7