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FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

MESTRADO INTEGRADO EM MEDICINA

2017/2018

Ana Luísa Gomes Cardoso

Perturbação do Comportamento Alimentar Compulsiva, uma nova doença. Que tratamento? / Binge Eating Disorder, a new disease. Have we got a new treatment?

março, 2018

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Mestrado Integrado em Medicina

Área: Psiquiatria e Saúde Mental

Tipologia: Monografia

Trabalho efetuado sob a Orientação de:

Prof.ª Dr.ª Isabel Maria Boavista Vieira Marques Brandão

Professora Doutorada da FMUP

Trabalho organizado de acordo com as normas da revista:

International Journal of Clinical Neurosciences and Mental Health

março, 2018

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Projeto de Opção do 6º ano - DECLARAÇÃO DE INTEGRIDADE

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Projecto de Opção do 6º ano – DECLARAÇÃO DE REPRODUÇÃO

NOME

ANA LUÍSA GOMES CARDOSO

NÚMERO DE ESTUDANTE	E-MAIL
201201160	ana_cardoso27@hotmail.com

DESIGNAÇÃO DA ÁREA DO PROJECTO

PSIQUIATRIA E SAÚDE MENTAL

TÍTULO ~~DISSERTAÇÃO~~/MONOGRAFIA (riscar o que não interessa)

"BINGE EATING DISORDER, A NEW DISEASE. HAVE WE GOT A NEW TREATMENT?"

ORIENTADOR

ISABEL MARIA BOAVISTA VIEIRA MARQUES BRANDÃO (PROFA DRA)

COORIENTADOR (se aplicável)

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Faculdade de Medicina da Universidade do Porto, 19/03/2018

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Dedicatória

Em primeiro lugar, gostaria de agradecer à Professora Doutora Isabel Brandão, pela orientação, apoio, disponibilidade e simpatia com que me acompanhou durante a construção deste trabalho.

Adicionalmente, queria agradecer à minha mãe, por todo o apoio, carinho, sabedoria e paciência, sem a qual nada do que tenho conquistado seria possível.

Binge Eating Disorder, a new disease. Have we got a new treatment?

Ana Luísa Gomes Cardoso[1]

Isabel Maria Boavista Vieira Marques Brandão[2]

[1]Final Year Student, Faculty of Medicine, University of Porto, Porto, Portugal

[2]Ph.D., Psychiatry Department, Faculty of Medicine, University of Porto, Porto, Portugal

Correspondence:

Psychiatry Department of the Faculty of Medicine, University of Porto

Address: Al. Prof. Hernâni Monteiro 4200-319, Porto, Portugal

E-mail addresses: ana_cardoso27@hotmail.com; isabelmbrandao@gmail.com

Key-words: Binge Eating Disorder; Obesity; Cognitive Behavioral Therapy; Mindfulness; Mindfulness-Based Interventions

Abstract word count: 250

The authors declare no conflict of interest.

Binge Eating Disorder, a new disease. Have we got a new treatment?

Abstract

Binge Eating Disorder (BED) is the most prevalent specific eating disorder in the world and its main feature is the binge consumption of high-calorie foods in a short period of time, without any compensatory strategies. BED patients show a large risk for obesity and its associated medical comorbidities, as for numerous psychiatric disorders. Negative affectivity, body image disturbance and stress are all possible triggers; however, these patients present with altered reward sensitivity, reflecting structural differences found in fMRI studies. The three main goals of treatment are achieving a reduction in binge-eating episodes, and, ultimately, abstinence; weight loss and remission of the comorbid psychiatric conditions. Serotonin-Selective Reuptake Inhibitors (SSRIs) are the best studied medication for BED; however, their use, both isolated and in combination with psychological-behavioral therapies, has been reported to have inferior results than the isolated application of Cognitive Behavioral Therapy (CBT), the current gold standard treatment for this disease. Nevertheless, with moderate remission rates and considerable drop-out rates, there is the imperative need to explore other therapeutic approaches for BED, either as an alternative or a complement to CBT. In the 1990s there began to emerge the presently called “third-wave” behavioural therapies, in which are included the Mindfulness-Based Interventions (MBIs), a set of programs that incorporate the recent concept of mindfulness to psychotherapy. In this review, there is presented the current evidence on the potential benefit of these new therapies to treat BED and what challenges there are to face in order for them to be recognized and implemented.

Key-words: Binge Eating Disorder; Obesity; Cognitive Behavioral Therapy; Mindfulness; Mindfulness-Based Interventions

List of Abbreviations:

DSM-IV - Diagnostic and Statistical Manual of Mental Disorders (4th edition)

EDNOS - Eating Disorder Not Otherwise Specified

BED - Binge Eating Disorder

DSM-5 - Diagnostic and Statistical Manual of Mental Disorders (5th edition)

AN – Anorexia Nervosa

BN - Bulimia Nervosa

fMRI – functional Magnetic Resonance Imaging

PFC - Prefrontal Cortex

DA - Dopamine

RCT – Randomized Controlled Trial

SSRIs - Selective Serotonin Reuptake Inhibitors

FDA – Food and Drug Administration

LDX - Lisdexamfetamine

CBT – Cognitive Behavioural Therapy

MBIs - Mindfulness-Based Interventions

MBCT - Mindfulness-Based Cognitive Therapy

MBSR - Mindfulness-Based Stress Reduction

MB-EAT - Mindfulness-Based Eating Awareness Training

MACBT - Mindfulness-Action based Cognitive Behavioural Therapy

MMEG - Mindful Moderate Eating Group

Introduction

Binge eating is a behaviour characterized by the uncontrolled consumption of an objectively large amount of food in a discrete period of time, as described by the American Psychiatric Association. The concept was first mentioned in the literature by Stunkard in 1959 [1] and was included in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) in 1994, inside the category of Eating Disorder Not Otherwise Specified (EDNOS) [2]. Only recently it has been distinguished as the core behavioural feature of Binge Eating Disorder (BED), a now distinct psychiatric diagnosis defined in the latest, fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [3]. According to the latter, for one to be diagnosed with BED, there must exist recurrent and persistent episodes of binge eating, at least once a week, during a minimum of three months, which are associated with a sense of loss of control [3]. This last aspect is often described by patients as an inability to stay away from food or to stop eating. Binge eaters usually consume high-calorie foods, rich in fat, and/or sugar [3].

BED is the most prevalent specific eating disorder, affecting 3.5% of adult women and 2.0% of adult men in the USA [4]. BED appears to occur with similar frequencies in most developed countries and the World Mental Health Survey estimated an average lifetime prevalence of BED at 1.9% across surveys [5]. BED usually firstly manifests itself in teenagers or young adults, but it can arise later, in adulthood [3]. Treatment-seeking individuals with BED tend to be older than ones with Anorexia Nervosa (AN) or Bulimia Nervosa (BN) [3]. Concerning gender prevalence, BED affects almost twice more women than it does men, although this difference is greater on other eating disorders [6].

Binge eating used to be thought mainly as a maladaptive behaviour characterizing Bulimia Nervosa (BN), which makes it the main differential diagnosis of BED [3]. However, both pathologies differ largely, as inappropriate compensatory manoeuvres, such as purging, excessive physical exercise and use of laxative medication, only occur in BN. Furthermore, BED patients present superior successful treatment and remission rates than BN and other eating disorders, and this greater prognosis exists even if no treatment is established. Also, these individuals, despite experimenting with feelings of body and weight shame between binge episodes, don't exhibit clear dieting restriction to lose weight, differing from those with BN [3].

One of the most important aspects of BED is its marked association with obesity, although BED can affect both obese and non-obese patients. This association is particularly strong within treatment-seeking patients, with BED affecting 4 to 8% of obese individuals and 30% of those who are also dieting [7].

Obesity in BED patients manifests itself differently when comparing with their non-BED counterparts, showing different ages of onset, eating patterns, severity and evolution; they present with greater weight and body shape concerns, role impairment, and higher frequencies of concomitant psychiatric disorders [8], with 67% to 79% of BED patients presenting with at least one lifetime comorbid psychiatric diagnosis, including depression, anxiety, manic-depressive disorders, posttraumatic stress, body dysmorphic disorders and substance abuse [9]. Incidentally, the craving and loss of control found in BED patients can be matched to the craving for psychotropic substances and the loss of control over their use seen in persons with addiction [10]. Indeed, it has been lately studied the potential concept of the term food addiction and the consequent potential treatment benefits of substance abuse targeted medications in BED, due to this found association [10]**.** Related to these likely co-occurring diagnoses is an elevated suicide risk, which is significant even after controlling for mood disorders, i.e. depression [11]. It's relevant to note that this psychiatric

comorbidity is related to the severity of the compulsive symptoms, and not to the degree of obesity [3].

Another crucial part of the disorder's comorbidity is the greater risk for obesity-associated medical pathologies, namely metabolic syndrome, diabetes mellitus and hypertension, which diminishes their quality of life and increases mortality [8]. The severity of the disease depends on the weekly frequency of binge eating episodes, furtherly acknowledging associated symptoms and the level of functional impairment [3].

There have been postulated various theories on the basis of the pathophysiology of BED, particularly the motive for binge eating behavior. The Affect Regulation Model regards bingeing as a way to decrease negative affectivity, a concept long known and described as emotional eating [12]. This remains the most common trigger for compulsive eating, whether followed by compensatory behaviours or not. BED patients report binge eating in order to improve mood and diminish stress and not for physical satisfaction [13]. However, after the short-term alleviating effect of this behaviour, comes negative self-evaluation and dysphoria [14].

Negative affectivity and stress can originate from multiple factors, and one of them may be the overconcern, or even shame, of one's own body shape or weight [15]. Body image disturbance, although not included in the diagnostic criteria for BED, might be an important component of the disease's psychopathology, influencing negatively the disease's prognosis [16], and a potential target for treatment [17].

Similarly, the Escape Awareness Theory suggests that binge eating is intended to avoid negative emotion [13]. On the other hand, the Cognitive Theory explains binge eating as a momentary escape from restricted eating [18]. However, one model considers the three theories mentioned above, the Dual Pathway Model, and it is crucial to understanding the key potential role of mindfulness-based therapies scrutinized later in this essay [19].

It's known that BED appears commonly in certain families, thus genetic predisposition may be important [3].

The current evidence shows that individuals suffering from this disease demonstrate unique traits that can be recognized clinically and by medical imaging, by means of functional Magnetic Resonance Imaging (fMRI). There has been established that these patients present with alterations in reward sensitivity, as evidenced by differential activation of reward-related brain areas upon stimulation with calorie-rich food cues. These results are accompanied by structural alterations in these same areas.

Not only have BED patients increased sensitivity to food reward, they present with alterations in generalized reward sensitivity, showing a global hypo responsiveness to non-food cues [20]. The only fMRI study that has examined non-food reward processing in this population, using monetary incentives, demonstrated a decreased ventral striatum recruitment in the BED obese group, when comparing to non-BED controls [21]. The ventral striatum region of the brain is crucial to both the engagement of goal-oriented behaviours and affective stance [22].

In conclusion, there is to confirm the hypothesis that these individuals have diminished responses to wide-ranging stimuli which might represent a susceptible state that can be temporarily overcome by the ingestion of palatable foods.

One of the elements that help to define compulsivity, with its various forms of manifestation, in which is included pathological overeating, is the inability to stop the continued behaviour despite its aversive consequences [23]. This trait reflects a lack of inhibitory control processes which, in turn, are regulated by the prefrontal cortex (PFC) and cortico-striatal circuitries [24]. This is one common feature between BED and substance addiction, among other shared psychological, emotional, behavioural and genetic traits [25].

There have been defined two opposing systems when it comes to reward processing and inhibitory control functions: the “GO” system, comprising the dorsolateral PFC, anterior cingulate cortex and orbitofrontal cortex and the “STOP” system, contemplating the ventromedial PFC. During binge eating episodes, the first component is sensitized while the latter is compromised [26]. The role played by these brain regions in value representation and consequent choice behaviour makes it easy to understand the main behavioural features of the disease [20].

Another trait that distinguishes BED patients from their healthy peers is their different perception and expression of emotions and their differential use of emotion regulation strategies, both adaptive and maladaptive (reappraisal, acceptance, avoidance, rumination, suppression, among others) [11]. Summarizing, the main impairment they present is the shortage of adaptive strategies to deal with negative affectivity [27]. They have greater suppression mechanisms while their reappraise is diminished [28]. Rumination concerning the comparison of one’s present circumstances to ideal expectations, especially when it involves body image, seems to increase negative mental and emotional stances, and it might be correlated with the disease’s severity [29].

There are also particularities in various neurotransmitter systems co-occurring with binge eating in BED patients, with differential activities in the dopaminergic, serotoninergic, acetilcolinergic and endogenous opioid systems. Food intake is partially regulated by brain circuits involved in pleasure, motivation and positive behaviour reinforcement, thus these alterations are noted in reward-associated brain areas [30]. Animal models of binge eating suggest that bingeing on sugary or fatty diets causes a repeated release of dopamine (DA) in the Nucleus Accumbens and consonantly, BED patients demonstrated expressively greater extracellular DA levels in the caudate nucleus in response to food cues, comparing with non-BED obese controls [31, 32]. Raclopride, a DA antagonist, has shown to reduce food intake, although with

differential results according to the macronutrient consumed [33]. Laboratory experiments on the aforementioned models have shown that opioid receptors' antagonists reduce food intake [33]. Serotonin has been associated with satiety and, therefore, to weight loss. Acetylcholine levels peak at one's full feeding state [34]; however, its release is delayed with bingeing [35].

With its recent distinction as a main diagnostic condition, BED is starting to be established as a significant public health problem, not only due to its greater relative prevalence when compared to other longer recognized and better studied eating disorders, i.e. AN and BN, but also due to its associated substantial medical, psychological and social burden. Therefore, the importance of a soon effective treatment solution that covers both dimensions of this disease.

Development

The three main goals in the treatment of BED are achieving a reduction in the frequency of binge episodes, and, ultimately, abstinence, promoting sustained weight loss, and treating the coexistent psychiatric disorders (e.g., increasing positive mood, attenuating undue self-image concerns). Of the scales used to provide knowledge on the severity of binge eating, reference to the Binge Eating Scale [36] and the Eating Disorder Examination Questionnaire [37]. In some studies, emotional eating might be addressed, through the Dutch Eating Behaviour Questionnaire [38] and the Three-Factor Eating Questionnaire [39], for example.

The most commonly tested outcomes are the frequency of binge eating episodes, the primary outcome measure in nearly all Randomized Controlled Trials (RCTs), weight loss and treatment completion rates, which reflects treatment tolerability [40].

Pharmacotherapy

Antidepressants, antiepileptics, anti-obesity agents, “anti-craving” agents and stimulants classically linked to Attention Deficit Hyperactivity Disorder, have all been tested as isolated treatments for BED [40].

Selective Serotonin Reuptake Inhibitors (SSRIs) are the best studied medication for BED, perhaps due to the demonstrated efficacy and consequent approval by the Food and Drug Administration (FDA) of fluoxetine for BN [41]. Fluoxetine, fluvoxamine, sertraline and citalopram have been shown to expressively reduce the number of binge eating episodes and to promote weight loss in BED patients [42, 43], while studies with escitalopram have shown mixed results [44]. Despite their short-term ability to reduce symptomatology, binge-eating abstinence rates did not differ significantly from placebo with these medications [42]. Furthermore,

one systematic review was explicit on the lack of sufficient evidence to propose antidepressants as first line of treatment [45].

Atomoxetine, a norepinephrine reuptake inhibitor, has shown significant reductions in binge-eating episode frequency, binge day frequency, weight as well in a number of secondary outcomes, such as severity of illness, obsessive-compulsive symptomatology and hunger. Most importantly, some patients reached binge-eating remission with atomoxetine [46].

Along with its efficacy in significantly decreasing binge eating frequency and, more notably, achieving binge eating remission, topiramate is, currently, the medication to induce the most substantial weight loss in patients with BED. However, its high adverse event and dropout rates are to be taken in account [47]. Zonisamide is another antiepileptic drug known to have positive results on weight loss. Despite being efficacious in reducing binge eating episode frequency and body weight, it didn't induce binge remission and it was not well tolerated, with patients referring physical, psychological and cognitive impairment [48]. Lamotrigine, with the exception of weight loss and metabolic parameters, did not differ from placebo in any of the outcomes tested [49].

Lisdexamfetamine (LDX) is the prodrug of d-amphetamine and the first medication to be approved by the FDA for the treatment of moderate to severe BED, as it proved superior to placebo in both primary and secondary binge-related outcomes, from baseline [50]. The long-term results were consistent with its continued use [51]. It's important to mention that LDX is not, however, indicated for weight loss [52].

There have been very few studies testing anti-obesity medications for BED, i.e. orlistat, but, as expected, orlistat significantly improved weight loss but did not prove to be efficacious in reducing binge eating frequency, even when added to Cognitive Behavioural Therapy (CBT) [53]. Other medications have been tested, such as chromium picolinate, for its glucose regulation proprieties [54] or armodafinil, that showed optimistic results, albeit in small sample sizes [55].

The literature on pharmacological treatment solutions for BED remains limited, as the majority of the studies on this subject have been projected in very small, non-diverse samples, with short follow-up times [4]. There is a large collection of non-RCT studies on this matter as well, therefore disabling comparisons with placebo, which plays a major role in mental-illness populations. Long before the launch of the DSM-5 criteria for BED, Cooper Z. et al were already recognizing that the concept of BED as it was postulated in DSM-IV was a contributor to heterogenous research samples, which were including non-BED patients [56]. The overwhelming amount of pharmacotherapy studies existing currently were made prior to DSM-5, and, therefore, that can be another limitation to their results.

Cognitive Behavioral Therapy

Treatment approaches comprising pharmacotherapies only, particularly SSRIs, were shown inferior to CBT in the treatment of BED, which makes the latter the current gold standard treatment for this disease [57]. CBT has shown important reductions in binge-eating frequency and improvements in self-evaluation, mood and coping mechanisms [58]. However, it showed no influence on weight or weight-related quality of life [58, 59]. Remission rates range from 40 to 60%, meaning about 50% of patients remain symptomatic after therapy [57]. Average drop-out rates are of 25% [60].

Pharmacotherapy + CBT

The outcomes achieved with combination approaches, adding pharmacotherapy to behavioral therapies, i.e. CBT, were superior to those of medication alone, but inferior to the isolated application of CBT [61].

Nevertheless, some studies have shown a few exceptions. Topiramate has potentialized the results achieved with CBT, with less dropout rates [62]. The addition of zonisamide produced higher reductions of binge episodes and greater weight loss [63].

"Third-wave" behavior therapies and the concept of mindfulness

Hayes et al. have described the field of behaviour therapy as three overlapping historical generations or "waves" [64]. The first generation was born in the 1950s, disrupting with the psychoanalytic model, dominant at the time [65, 66]. The second generation corresponds to CBT, recognizing the role of language and cognition in psychopathology and continues to be the leading therapy approach through the present day [67].

The "third-wave" behavioural therapies began in the 1990s and are, for the past decade, gaining increasing exposure and scientific interest [64, 68]. Despite keeping in mind many concepts from CBT, they target one's experience of certain emotions and cognitive processes, and not their content [69]. Therefore, it is promoted a non-judgmental, open and accepting attitude towards aversive internal experiences, may they be thoughts, feelings, experiences or beliefs, without trying to diminish or avoid them [66]. These set of skills can be comprised into a concept named mindfulness.

Although the concept of mindfulness has its ancient origins in the Hinduism and Buddhism philosophies, only for the past two decades mindfulness techniques have seen cultural and scientific interest growth, particularly in the field of behaviour therapy [68]. Due to the recent appearance of the term in the psychology and psychiatry dictionaries, the precise meaning and underlying concepts of mindfulness are still difficult to define [66]. Ellen Langer was the first psychologist to describe mindfulness, referring to it as a “limber state of mind” [70]. However, the words used by mindfulness pioneer Jon Kabat-Zinn have become the most popular among authors: “paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally” [71]. This definition, widely used today, gave us the key ideas of awareness and acceptance of all immediate, internal experiences, the positive ones and the undesirable ones [66]. Skills developed under these conceptions aim to decrease emotional and cognitive reactivity and increase self-acceptance, by encouraging feelings of compassion and forgiveness towards oneself and others [66]. Individuals are trained to notice distressing sensations, to learn how to deal and tolerate them, without mistaken it for hunger, therefore decreasing reactive, automatic, unwanted responses [72].

The efficacy of mindfulness-related and/or acceptance-based techniques, has been studied and tested for innumerous psychiatric conditions, specifically depression, anxiety, substance abuse and PTSD, proving to be potentially beneficial in various RCTs [73, 74]. Additionally, many of these interventions are being exponentially tested as a treatment complement in medical, long term, high-comorbid conditions (i.e., cancer, chronic pain, neurologic disorders) [74, 75].

Under the third-generation group of therapies fall the Acceptance and Commitment Therapy (ACT), the Dialectical Behaviour Therapy (DBT), the Compassion Mind Training/Compassion-Focused Therapy (CFT), the Functional Analytic Psychotherapy (FAP), the Behavioural Activation (BA), the Metacognitive Therapy (MCT) and the Mindfulness-Based Interventions (MBIs) [76]. The difference between these programs is the dose of mindfulness training each one implements [77]. MBIs are primary mindfulness interventions, meaning they contain mindfulness training in every session of treatment; others incorporate mindfulness into a multi-component treatment approach [77]. Some of these therapies can be widely applicable among medical and non-medical conditions, while others focus on specific populations; some can be potentially dynamic, resulting either in the context of individual psychotherapy or group sessions [19]. While previous reviews have shown effectiveness of programs containing some mindfulness context in reducing binge eating, very few have tested MBIs for the same application [78]. Therefore, this essay will focus mainly on the potential therapeutic effect of MBIs.

MBIs can be aggregated into two main programs, the Mindfulness-Based Cognitive Therapy (MBCT) and the Mindfulness-Based Stress Reduction (MBSR), that can be applied as they were originally concepted or be modified to address multiple conditions, including binge eating behaviours [19].

Mindfulness state and awareness of individuals can be measured through scales, i.e. the Mindful Attention Awareness Scale [87], the Toronto Mindfulness Scale [88], the Five Facet Mindfulness Questionnaire [78], among others. The Mindful Eating Questionnaire, as the name suggests, is used to measure mindful eating [89].

MBSR was created by Kabat-Zinn and colleagues and is the first contemporary model in psychology to incorporate the concept of mindfulness, originally developed and used in the context of chronic medical conditions [79]. It defends the sustained practice of mindfulness meditation, incorporating elements of Hatha Yoga, the most popular yoga system in the world, i.e. dynamic posture sets and breathing exercises. Increased, sustained awareness must apply to all internal signals, physiological, physical, cognitive and emotional, especially those who trigger binge [79]. Adapted formats include the Mindfulness-based Eating Awareness Training (MB-EAT), considered the first attempt to apply mindfulness training specifically for BED patients. This program incorporates elements of mindfulness meditation, mindful eating, self-acceptance, compassion and forgiveness [80]. Although there is no established definition for mindful eating, it consists of paying close attention to the physical experience of eating, observing the physical and emotional sensations that it causes, particularly noting sensations of hunger and satiety; eating all types of food, while making conscious choices; eating slower and gaining insight into what triggers their compulsion [72]. From then, MBSR has been adapted to non-binge, obese patients [81].

The MBCT integrates knowledge from CBT and MBSR therapies. The CBT component of these programs focuses on dietary restraint and planned, regular eating patterns, relying on self-monitoring and exploration of binge-eating triggers [19]. According to patient population, there were created the following therapies: the Modified MBCT for binge eating, the Mindfulness-Action based Cognitive Behavioural Therapy (MACBT), aimed at both BED and Substance Use Disorder (SUD) patients, the MBCT protocol adapted for the post-bariatric surgery population and the Mindful Moderate Eating Group (MMEG) [19]. The MMEG was created in 1994 and rewritten in 2005 to incorporate mindfulness training [82, 83]. There were found substantial and sustained reductions in binge eating frequency and severity, emotional overeating, restrictive eating and poor body image with the implementation of this program [84].

Mindfulness focuses on gaining, or increasing, emotion control, improving one's self-perception and self-compassion and decreasing dysphoric symptoms, such as anxiety and depression, either towards the self or their interpersonal relationships, which, as mentioned before, are in the background of the development of eating disorders, e.g. BED [19, 66]. Thus, the relevance of mindfulness in the treatment of these individuals.

Despite the established program, when testing for the potential benefit of these therapies in the context of disordered-eating behaviors, particularly binge eating, in the presence or absence of diagnostic criteria, researchers found not only a significant reduction in bingeing frequency [78, 85] but also in emotional and external eating [86]. Also surprising was discovering that a lesser degree of conscious control over their eating behaviors, made patients feel they had more control over their eating [85]. However, the amount of time one expended in meditation didn't relate to the reported final sense of mindfulness [85].

When it comes to weight loss, unless this is the main goal of treatment and supplemental weight-related strategies are implemented, mindfulness training, on its own, doesn't show consistent, positive results [77, 90].

The very few studies that have compared these therapies with CBT show a similar or, to some extent, greater response with the first mentioned group [77, 91]. When combining them both, mindfulness skills were considered the most helpful part of the treatment by patients, reducing drop-out rates seen with CBT alone [84]. Unrelated to the eating components of the treatment, but specifically due to the mindfulness practice alone, patients recognized feeling happier and healthier with themselves and in their relationship with others [84].

Improvement on primary and secondary outcomes remained sustained a few months after treatment [77, 84]; however, nothing can be inferred yet about long-term remission, since follow-up times are still short [77].

We are standing before a new and exciting area of scientific research, particularly for those passionate about behavior therapy, where there is still much room for improvement. Therefore, investigation is increasing. Portuguese researchers developed a new, innovating approach for BED, called the Befree program, which integrates mindfulness, psychoeducation and self-compassion skills [92]. The results are promising, as BED was eliminated up to 6-month post-intervention [92].

Discussion

Obesity is one of the most worrying, growing diseases in the world and is known to be caused by an imbalance in energy intake and energy expense. BED, the most frequent eating disorder, has become an important cause of obesity, as it increases energy intake.

Despite being successful in reducing symptomatology and exploring development causes for the disease, CBT is still ineffective in about 50% of patients, and its discontinuation rates are to take into account, as 25% of patients don't find any benefit in this therapy.

Mindfulness and acceptance-based programs are a new, promising solution for these individuals. However, some challenges must be overcome.

In accordance to their relatively recent appearance in the literature, most of the evidence support existing today is based on limited, experimental or observational studies [19]. Therefore, current evidence is still based on small sample sizes, non-comparative, short-term analyses, variable intervention components and primary outcomes [19, 77]. Also relevant is the fact that a lot of the studies on the subject were developed before the fifth edition of DSM, including patients that may not fulfil BED criteria and, thus, not represent this population adequately [19]. Additionally, most BED patients seeking treatment are obese and so is the main study population; thus, non-obese, BED patients cannot infer anything about treatment outcomes.

With future, greater research, that is, with a randomized, controlled design, with larger samples and longer follow-up times, MBIs may prove important and needful in the treatment of patients with BED, as existing research already shows its effectiveness and acceptability.

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Anexo 1 – Normas de publicação da revista **International Journal of Clinical Neurosciences and Mental Health**

As an open-access, online-only publication, the International Journal of Clinical Neurosciences and Mental Health does not enforce arbitrary word count or illustration limits. The journal a provides a recommendation on the length of manuscripts, but authors are welcome to submit manuscripts outside those recommendations if deemed appropriate.

Reviews and Drug Reviews

Review articles on current topics related to psychiatry, mental health, medical psychology, neurosurgery and neurology, as well as CNS-related drugs are welcome. Both invited and unsolicited submissions are accepted. Review articles are recommended to have up to 5000 words (excluding title page, abstract, acknowledgements, references and tables.). Inclusion of newly designed figures and tables to summarise key points is encouraged. The used of previously published material is subject to the licence agreement of the original publisher and should generally be avoided. If previously published materials are, nonetheless, included in the illustrations, the authors should procure appropriate authorisation for use from the original publisher prior to submission.

Manuscript Submission

These instructions advise on how the manuscript should be prepared and submitted. Manuscripts that do not comply with the guidelines will be returned to the authors before being considered for peer-review.

All manuscripts should be prepared in A4-size or US-letter size, in UK or US English throughout the manuscript, a mixture of UK and US English will not be accepted.

Manuscripts should be submitted in *.doc and *.pdf formats, in the appropriate section of the journal website: IJCNMH online submission.

Manuscript Preparation

The manuscript must be divided in 2 files: the Title page (submitted in *.doc format and *.pdf formats) and the Manuscript body (submitted in *.doc and *.pdf formats).

Submitting these 2 files is essential to ensure double-blind peer-review. Failure to provide these 2 files will result in delay in the peer-review process, since the manuscript will be returned to the authors for adjustment.

Title page

This should be submitted as a separate file from your manuscript (to ensure anonymity in the peer review process) and should include:

- Article title.
- Authors' names, titles (e.g. MD, PhD, MSc, etc.) and institutional affiliations.
- Corresponding author: name, mailing address, telephone and fax numbers, email address.
- Keywords (maximum of 10), according to MeSH terms, whenever possible.
- A short title (running head) (up to 70 characters).
- Abstract word count (up to 250 words).
- Disclosure of conflicts of interest. Any conflict of interests should be declared. If authors have no declaration it should be written: "The authors declare no conflict of interest".

Manuscript body:

The Manuscript body must be anonymous, not containing the names or affiliations of the authors. It must be structured in the following order: title, abstract, body text, acknowledgements, references, tables, and figures captions/legends. The manuscript body should contain the title and the abstract, since the title page is not sent to reviewers during peer-review.

- The text must be formatted as follow:
    - Arial fonts, size: 11 points.
    - Double line spacing (see paragraph menu).
    - Aligned to the left (not justified).

Showing continuous line numbers on the left border of the page. For MS Word you can add line numbers by going to: Page Layout -> Line Numbers -> select “Continuous”; for OpenOffice: Tools -> Line Numbering -> tick “Show numbering”.

Title

A descriptive and scientifically accurate article title should be provided.

Abstract (250 words maximum)

An abstract should be prepared for all types of manuscript, except Editorials.

Systematic review articles should have a structured abstract with generally the same headings as Original Research articles, whereas narrative review articles can have a structured or unstructured abstract, as deemed appropriate by the authors.

Abstracts for Viewpoint articles and Letters to the Editor, can have structured or unstructured abstracts, as deemed appropriate by the authors.

Body text

Review articles and Drug Reviews

These types of articles should be organised in sections and subsections, as deemed appropriate by the authors.

Acknowledgements

This section should name everyone who has contributed to the work but does not qualify as an author. People mentioned in this section must be informed and only upon consent should their names be included along with their contributions. Financial support (with grant number, if applicable) should also be stated here.

References

References citation in the text should be numbered sequentially along the text, within square brackets. The use of a reference management tool (such as Endnote or Reference Manager) is recommended. References must be formatted in Vancouver style. Only published or accepted for publication material can be referenced. Personal communications can be included in the text but not in the references list.

Nomenclature

All units should be in International System (SI). Drugs should be designated by their International Non-Proprietary Name (INN).