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Cause and treatment of anorexia nervosa

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Abstract

The hypothesis that eating disorders are caused by an antecedent mental disorder, presently believed to be an obsessive compulsive disorder, has been clinically implemented during many years but has not improved treatment outcome. Alternatively, eating disorders are eating disorders and the symptoms of anorexic patients and probably bulimic patients as well, are epiphenomena which emerge as a consequence of starvation. This hypothesis is supported by the observations of the effects of a 6 month long period of semi-starvation on healthy human volunteers, which demonstrated not only the emergence of psychiatric symptoms but also the reduction in eating rate which is typical of anorexia nervosa patients. On this framework training anorexic patients how to eat may be a useful intervention. We report that anorexic patients, either with a body mass index <14 or >15.5 display the same pattern of eating behavior, with a low level of intake, a slow eating rate and a high level of satiety. They also have the same, high level of psychiatric symptoms, including obsessive compulsive symptoms. Training patients to eat more food at a progressively higher rate reverses these symptoms and patients remain free of symptoms during an extended period of follow-up. It is suggested that the pattern of eating behavior mediates between the starved condition and the psychopathology of anorexia nervosa.

Keywords: Anorexia; Eating behavior; Psychiatric symptoms

1. Introduction

Eating disorders, including anorexia nervosa, bulimia nervosa and eating disorders not otherwise specified, are considered chronic psychiatric disorders which are difficult to treat and, most likely for these reasons, they are also believed to be multifactorial disorders or unknown etiology [1]. We first review the prognosis, outcome, treatment and current theories of the causes of eating disorders. Because outcome has not improved significantly over a considerable period of time, we offer an alternative framework of the cause of eating disorders and outline its clinical implementation. The major difference between patients with anorexia nervosa and bulimia nervosa is that anorexics are underweight but bulimics are normal weight. Most, if not all, other aspects are similar and it seems likely that anorexia and bulimia are two phases of the same disorder. Our discussion will concentrate on anorexia.

2. Prognosis, outcome and treatment

The published prevalence of anorexia nervosa varies between 0 and 1% and is about 0.3% on average and the age of onset of the disorder is 14–19 years [2]. Most patients (95%) are females. The chance of recovery is less than 50% in 10 years, about 25% remain ill and the mortality varies between 0 and 25% [3]. While weight restoration of malnourished anorexics is manageable, relapse is a problem [4]. These findings are the basis for the view that anorexia nervosa is a chronic disorder. This distressing scenario has not changed in 50 years [3].

Many anorexics display bulimic behavior and most bulimics have a history of anorexia. And so it is neither surprising that the prevalence for bulimia is about the same as that for anorexia nor that bulimic patients are older than anorexic patients [2]. Although the situation for patients with bulimia nervosa is considered less severe than that for anorexics, outcome in bulimia is also poor [5].

Guidelines for the treatment of patients with eating disorders have recently been launched in many countries (e.g., [6]) and these are based on the available scientific evidence. In the case of anorexia nervosa, the guidelines are based on very weak evidence. For example, “the only evidence that anything works in adult anorexics” is a study in which cognitive behavioral

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therapy reduced the rate of relapse from 53 to 22% [4]. A review of 5512 studies on the same topic found only six studies that fulfilled scientific criteria and out of these only two that indicated some effect of treatment [7]. Even this appears to be an overstatement. Thus, one of the studies [8] reported that 35% of the patients dropped out of treatment, that there was some response in the remaining five out of six patients in comparison with two patients in a control group and that 50% of the patients dropped out of the study upon follow-up 1 year later.

The scientific basis for the suggestion that family-based treatment is effective in children with anorexia nervosa is a randomized controlled trial [9] and a follow-up of the results 5 years later [10]. In these studies, 6 out of 10 patients had a good outcome compared to 1 out of 11 in the control group. Upon follow-up, all patients, regardless of treatment, had improved and the authors concluded that their results could be "attributed to the natural outcome of the illness", rather than to the treatment [10]. Subsequent studies on the same topic have yielded similar results.

It is often claimed that cognitive behavioral therapy is effective in bulimia nervosa [1] and this type of treatment is therefore considered standard of care for bulimia in many countries. This also seems to be based on weak scientific evidence. Thus, a comprehensive review concluded that "there is a small body of evidence for the efficacy of cognitive behavior therapy in bulimia nervosa and similar syndromes, but the quality of trials is very variable and sample sizes are often small" [11]. A recent series of papers [12,13] has clarified the issue. Out of 194 patients who entered treatment, 54 (28%) dropped out or were withdrawn and only 58 (30%) of the 140, who completed treatment, went into remission. Upon examination 4 months after treatment, 21 (44%) out of 48 (ten could not be located) had relapsed. Thus, only 27 (14%) out of 194 patients who entered cognitive behavioral therapy bulimia were in remission 4 months after treatment.

The evidence that psychopharmacological treatment is effective in treating eating disorder patients is also weak [14].

We suggest that the reason why currently used treatments for eating disorders are ineffective is because they are based on erroneous assumptions and are often incompatible with well known facts in neurobiology. We outline these assumptions in the following paragraphs.

3. Current explanations of eating disorders

According to a main explanatory model for the development and maintenance of eating disorders, there is a mental disorder that predisposes an individual not only for anorexia but also for bulimia. The mental disorder is believed to have a genetic basis and an alteration in a brain transmitter system is thought to mediate the expression of the eating disorder [15,16]. While this hypothesis has been extensively tested, it has not yet yielded clinically useful results. In the following, we suggest a reason why.

4. Obsessive compulsive disorders and anorexia nervosa

While there have been many suggestions as to what kind of mental disorder causes anorexia (and bulimia), the hypothesis has recently been specified. Thus, it has been suggested that "childhood anxiety represents one important genetically mediated pathway towards the development of anorexia nervosa and bulimia nervosa" and that this is reflected in onset of obsessive compulsive disorder (OCD) before anorexia [15]. (We refer to this "genetically mediated pathway" as "genes" below.) A test of this hypothesis yielded the following results. Out of 94 patients with anorexia nervosa, 35% also had OCD. Upon examination of these, about 12% dropped out and of the remaining, 23% had OCD before they had anorexia nervosa. Thus, $94 \times 35\% \times 88\% \times 23\% = 7$ individuals out of 94 (7%) had OCD before they had anorexia nervosa [15]. As the majority of the patients had OCD simultaneously with anorexia nervosa, these data show that the expression of OCD before anorexia nervosa is rare.

The incidence of OCD increases exponentially when an individual approaches puberty with no difference between the sexes [17]. We must assume, therefore, that the major expression of the hypothesized genes for OCD and anorexia occurs simultaneously with the onset of anorexia or later and that the genes are expressed as anorexia only in girls (the prevalence of anorexia is very low in boys), but as OCD in both girls and boys. However, it was suggested that the genes may be expressed not only as OCD but as other anxiety disorders as well and that these disorders have a life time prevalence as high as 12–18% or even 30% [15]. Whether genes with such time-dependent, sexually dimorphic and phenotypically diverse expression patterns exist will be difficult to investigate.

Furthermore, while it is apparently possible to diagnose OCD retrospectively already at 5 years of age, it appears that childhood OCD is 8–12 times more prevalent in the USA (reported prevalence: 2–3%) [15] than in England (reported prevalence: 0.25%) [17]. If OCD causes anorexia, one would expect anorexia nervosa to be about 10 more prevalent in the USA than in England. There is no evidence that this is the case.

Another problem is that it is difficult to understand how the brain mechanisms which are involved in OCD might activate those that mediate the altered eating behavior of eating disorder patients. Thus, while the orbitofrontal and anterior cingulate cortex and the basal ganglia may play a role in OCD [18], their role in eating behavior is unclear. The neurobiology of eating engages mainly hypothalamic and brainstem regions [19]. The orbitofrontal cortex houses the secondary taste cortex and is concerned with the reward value of different taste, smell and visual stimuli and also has a role in learning [20], but we do not know if these functions are related to disordered eating behavior.

5. 5-hydroxytryptamine and anorexia nervosa

It has been suggested that the neurotransmitter system mediating the expression of anorexia nervosa (and bulimia nervosa) is 5-hydroxytryptamine (5-HT). This hypothesis was first tested by measuring the concentration of 5-hydroxyidol-acetic acid (5-HIAA), a metabolite of 5-HT and an indirect measure of the turnover of brain 5-HT, in the cerebrospinal fluid (CSF) of anorexic patients. One must obviously be cautious in