Severe and enduring Anorexia Nervosa: a brief narrative review about the concept and its therapeutic options

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Abstract

Anorexia Nervosa (AN) is a severe psychiatric disorder that can present in a chronic and durable form, often named severe and enduring AN (SE-AN), with little available literature considering therapeutic options in this subgroup of patients. We aimed to perform a bibliographic review considering articles about severe or chronic forms of AN published in the last ten years. According to the analyzed data, there are different definitions in the studies concerning SE-AN, however, many authors consider 7-years of disease as a threshold for diagnosing SE-AN. In the future, it will be important to have a standardized definition of SE-AN in order to characterize its preferential approach in large scale studies. Regarding therapeutic options, cognitive-behavior therapy remains a valuable option in these patients, despite the need of some adaptations considering the high probability of past failed psychotherapeutic approaches. Regarding biological therapies, there is now exploration of new possibilities such as the use of transcranial magnetic stimulation and deep brain stimulation in these patients. However, research towards these approaches is still in its beginnings, with need for further studies to characterize their possible role.

Keywords: Anorexia nervosa, Severe, Enduring, Chronic, Resistant
Introduction

Anorexia Nervosa (AN) is a severe psychiatric disorder which clinical presentation includes both physical and mental manifestations. It can present in variable ways, such as forms often defined as severe and enduring AN (SE-AN). SE-AN is a concept that includes different subgroups of patients with AN, however, the most common used criteria are the ones according to the duration of illness, defining patients with SE-AN as having at least 7-years of the disorder and also having the experience of previously failed treatment attempts [1]. There has been considerable progress concerning the treatment of younger patients with shorter illness duration, however the preferential approach towards patients with SE-AN has received less attention, despite the fact that its sufferers maintain high levels of disability concerning different domains, namely in terms of employment and family burden [2].

In this paper, the authors conducted a bibliographic search in the Medline database on December 22nd, 2018, using the terms “severe enduring”, “chronic”, “resistant” and “anorexia nervosa” published in the last 10 years. The initial search resulted in 391 articles, and 14 were included in the final version of the review, with the choice of articles based on selecting those specifically addressing severe, chronic or resistant samples of patients with AN. We aimed to analyse the conceptualization of the entity known as SE-AN, as well as the impact on its sufferers, also trying to summarize the therapeutic approaches that have been explored in this population.

Conceptualization of SE-AN

As stated before, SE-AN is usually defined as a clinical picture of AN with a duration of at least 7 years and failed past attempts of treatment. However, according to a systematic review about articles concerning the labeling of SE-AN, the definition varies significantly across different samples. Although illness duration is commonly the preferred criteria to define SE-AN, some authors use criteria such as failed previous treatment approaches, low body mass index (BMI), impact on patient functioning and low motivation to change [1]. As stated in a cross-sectional study with 355 patients with AN, severity and enduringness are dimensional concepts, not always correlated with each other, and patients with AN can present at different points of that spectrum [3].

It is usually reported that due to the disability to the work that SE-AN causes, patients place a significant burden on their families and welfare system. Also, they experience poor quality of life [4]. In a qualitative study with 8 patients with 20–40 years of AN and a mean BMI of 15.7, difficulties were reported in various domains, including psychological, social and family life, as well as occupational and physical problems. Feelings of unworthiness and self-loathing were common, as well as frugality and a tendency to delay reward. However, some patients showed signs of resilience and pride at their achievements, looking at the ED as a mean of superiority towards others [5].

Therapeutic approaches in SE-AN: Psychotherapeutic approaches

It has been described that in AN, a long duration of illness before treatment is an unfavorable prognostic factor, and that there are high drop-out rates in patients with SE-AN, leading to the suggestion that conventional treatments such as Family Based Therapy (FBT) or Cognitive Behavioral Therapy (CBT) may misalign with the patients’ expectations. However, in a comparative study between patients with AN and SE-AN treated with enhanced-CBT (CBT-E), both groups showed similar improvements in BMI, eating disorder and general psychopathology during treatment and at a 12-month follow-up [4].

In another trial, with 66 patients with SE-AN, patients were randomized to receive CBT-AN or specialist supportive clinical management. The authors found a retention rate of 85% and found no differences between groups at end-of-treatment, however, at a 6-month follow-up evaluation the CBT-AN group showed higher score on Weisman Social Adjustment Scale and at 12 months had lower Eating disorder Examination (EDE) global score and higher readiness for recovery [6]. Considering the same sample of patients, in a secondary analysis concerning therapeutic alliance (TA), the only significant predictor of TA were the patients expectations for treatment, contrasting with previous data suggesting that increased duration or severity of illness and decreased motivation may have negative impact on TA. These data highlight the importance of increasing patients’ expectations about the intervention in the beginning of treatment [7]. Still considering the importance of therapeutic alliance in this sample, early TA was a significant predictor of restraint and shape concern at follow-up, and late therapeutic alliance was a significant predictor of weight change, depressive symptomatology and ED symptoms at the end of treatment and follow-up [8]. Considering these data, CBT directed to SE-AN may need adaptation, namely building a TA longer before engaging in more active therapeutic strategies, in order to retain the patients in treatment, increased flexibility, understanding and compassion in relation to the issues these patients face, while being able to maintain the focus of CBT [9].

Therapeutic approaches in SE-AN: Biological approaches

Recently, research in the field of SE-AN has turned towards new possibilities, including the recourse to transcranial magnetic stimulation (TMS) [2]. Regarding TMS, a case report of two patients with long standing AN, one with 12 years of illness and the other with 35 years of illness, treated respectively with 20 and 19 sessions of TMS.
applied to the left dorsolateral prefrontal cortex, there was an improvement in ED symptoms and mood after the completion of the sessions and at 1-month follow-up, despite the absence of improvement in BMI. These results suggest that TMS may have some value as an adjunctive treatment in SE-AN, requiring further studies [10]. In a recent randomized double-blind controlled trial, the authors compared real magnetic-resonance guided TMS versus sham in a group of 30 patients with AN with a duration of more than 3 years and at least one previous inpatient admission. The group receiving treatment, with 20 sessions of TMS over the course of 4 weeks, showed improvement in mood, while showing small effect size regarding BMI or ED symptomatology [11]. Deep Brain Stimulation (DBS) is also a possible therapeutic approach directed towards the treatment of SE-AN, as highlighted in a study protocol destined to use DBS in the nucleus accumbens in six patients with SE-AN [12].

Considering novel pharmacological options directed towards the treatment of SE-AN, dronabinol, a synthetic cannabinoid, was recently tested in a randomized controlled trial which included 24 women with AN of at least 5-years duration, randomized to treatment with either dronabinol followed by placebo or placebo and then dronabinol, in the dose of 2.5 mg of dronabinol twice a day. The authors observed that during treatment with dronabinol the patients significantly increased their weight, gaining an average of 0.73 kg. However, the authors did not evaluate possible psychiatric side-effects of the therapy with dronabinol highlighting the need of larger safety-based studies before considering dronabinol as an option for the treatment of SE-AN [13].

**Discussion and conclusions**

According to these data, it is clear there is great disability in sufferers from severe and chronic AN. In future studies, it will be important to have a clearer definition of SE-AN, due to the various implied concepts and illness time that different studies consider. Also, severity and enduringness are different concepts and while sometimes associated, that may not always be the case [3]. There is a need to define universal criteria, defining SE-AN in order to further the research in this population, including the definition of the optimal therapeutic approach [1].

Considering treatment approaches directed to SE-AN, CTB appears to show promise also in this population, despite the possibility of some adjustments considering the chronicity and previous attempts at psychotherapy that many of these patients have tried [9]. Recently, research has turned towards exploration of new possibilities, namely DBS and TMS. Up to this date, the only available evidence concerning these approaches are based on case reports, lacking large scale studies to better define their role in SE-AN. Also, ethical questions must be addressed in neurosurgical trials, namely questions related to the informed consent and capacity for decision [14].

**Abbreviations**

AN: Anorexia Nervosa; BMI: Body mass index; CBT: Cognitive Behavioral Therapy; CBT-E: enhanced-CBT; DBS: Deep Brain Stimulation; EDE: Eating disorder Examination; FBT: Family Based Therapy; SE-AN: Severe and enduring AN; TA: Therapeutic alliance; TMS: Transcranial magnetic stimulation

**Competing interests**

The authors declare that there are no conflicts of interests.

**References**


12. Park RJ, Scaife JC, Aziz TZ. Study Protocol: Using Deep-Brain Stimulation, Transcranial magnetic stimulation (rTMS) and a Tran-schanial magnetic stimulation (TMS) approach directed towards the treatment of SE-AN, dronabinol, a synthetic cannabinoid, was recently tested in a randomized controlled trial which included 24 women with AN of at least 5-years duration, randomized to treatment with either dronabinol followed by placebo or placebo and then dronabinol, in the dose of 2.5 mg of dronabinol twice a day. The authors observed that during treatment with dronabinol the patients significantly increased their weight, gaining an average of 0.73 kg. However, the authors did not evaluate possible psychiatric side-effects of the therapy with dronabinol highlighting the need of larger safety-based studies before considering dronabinol as an option for the treatment of SE-AN [13].