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The Importance of Restoring Body Fat Mass in the Treatment of Anorexia Nervosa An Expert Commentary

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ABSTRACT

Anorexia nervosa is a severe mental disorder that is characterised by dietary restriction, low weight and widespread endocrine abnormalities. Whilst the importance of weight restoration has been recognised in recent guidelines, the significance of normalising body fat mass has received less attention. A recent systematic review and meta-analysis found that a minimum of 20.5% body fat mass is necessary for regular menses in women with anorexia nervosa of reproductive age. This has significant implications for both treatment and research. It is important to help the patient and carers understand that a certain level of body fat percentage is essential for optimal health, such as the return of menstruation. Further research is needed into how best to use this information to help motivation to change as part of treatment. The benefit of the return of menstruation goes beyond improved fertility: it signals the normalisation of sexual hormones, which have a widespread impact on the body and multiple pathways in the brain. Given the complex functions of adipocytes in various organs of the body, the metabolic effects of the normal body fat tissue should not be underestimated. Further research is needed to elucidate the mechanisms behind the link between minimum body fat mass, menstruation, bone and brain health in anorexia nervosa.

Keywords: *Anorexia nervosa; body fat mass; adipocytes; menses; bone health*

Anorexia nervosa is a complex mental disorder that has major consequences for the patient's physical health. One of the main features of the disorder is the fear of fats, both in the diet and in the body. Patients avoid fattening foods, and their dread of fatness is a pervasive, intrusive, overvalued idea, which drives severe dietary restriction.[1] Unfortunately, the modern environment constantly reinforces these preoccupations, not just in terms of idealised slim images in advertising, but also through the promotion of low fat and diet products by the food and weight loss industries, to both adults and children.[2] Owing to their fear of weight gain or becoming fat, patients severely restrict their diet and develop malnutrition to various degrees.[3] The Diagnostic Manual of Mental Disorders (DSM-V) has aligned the severity categories of anorexia nervosa to the WHO malnutrition categories.[4] With malnutrition, there are widespread endocrine abnormalities: stress hormones increase and sexual hormones reduce.[5,6] Approximately 90% of patients with anorexia nervosa are female and they develop either primary or secondary amenorrhoea; indeed, this is included amongst the diagnostic criteria in the International Classification of Diseases (ICD-10).[1]

The mainstay of treatment of anorexia nervosa is psychological. The recent UK National Institute of Clinical Excellence (NICE) guidelines recommend Cognitive Behavioural Therapy for Eating Disorders (CBT-E), Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA), Standard Supportive Clinical Management (SSCM) or focused psychodynamic therapy for adults, and family therapy for children and adolescents.[7] However, in terms of effectiveness, there is no substantial difference between these therapies, and recovery can take a long time.[8,9] NICE also recommends that all psychological treatments should aim for normalisation of weight: "helping people to reach a healthy body weight or body mass index (BMI) for their age is a key goal and weight gain is key in supporting other psychological, physical and quality of life changes that are needed for improvement or recovery". This is an important recommendation, as there has been variation in practice in this respect until now. For example, the definition of recovery or remission in anorexia nervosa BMIs varies between 17.5 and 25 in different studies.[10,11] In most countries, patients are usually discharged from inpatient treatment before reaching normal weight, and relapse rates are high.[12,13] Furthermore, current psychological therapies, such as CBT-E,[14] SSCM or MANTRA,[15] do not directly address the need to restore body fat mass for normal endocrine functioning as part of treatment. This may be due to the fact that existing psychological models were developed without integrating recent understanding of the metabolic processes that may play a role in anorexia nervosa. Furthemore, the therapists' fear that directly addressing the need for restoring normal fat stores could harm engaging the patients may also contribute. Traditionally, the metabolic abnormalities were seen as the consequences of dietary restriction, rather than being potentially relevant to aetiology or maintaining factors. Furthermore, historically, fat tissue was regarded as passive energy storage. This view has been changing since the discovery of leptin and adiponectines in the 1990s;[16,17] and it has been recognised that adipose tissue has important metabolic functions, including energy intake and energy expenditure, insulin sensitivity, immunity[18] and bone health.[19,20] There are numerous adipose tissue-secreted signalling mediators, and the full details of the functions of these are yet to be understood.[16] Furthermore, the cellular structure and metabolic effects of adipose tissue differ according to its location: dermal, subcutaneous and visceral depots have very different roles to bone marrow, skeletal muscle or pancreas fat.

The significance of the loss of fat tissue has rarely been explored in the eating disorder literature. A notable exception is the description of

bone marrow abnormalities in anorexia nervosa.[21] However, recent genome-wide association studies indicate that there may be underlying metabolic vulnerability in anorexia nervosa relating to glucose and lipid metabolism and low BMI, which are likely to be related to adipose tissue.[22] The findings of a recent large longitudinal study are consistent with this: the average growth trajectory for individuals with later anorexia nervosa was significantly below normal as early as 4 years of age for girls and 2 years for boys, suggesting that a low BMI may be an important early sign of the emerging disease process many years before the clinical manifestation.[23]

El Ghoch is one of the leading researchers exploring the significance of body composition, including lean skeletal body and fat mass in patients with anorexia nervosa.[24–29] In the current systematic review and meta-analysis, his team has found that patients whose menstrual cycles returned had a higher body fat mass than those who remained amenorrhoeic. On average, about 20.5% minimum body fat mass is necessary for regular menses in women of reproductive age. From an evolutionary perspective, the shutting down of the reproductive system in times of food shortages is adaptive: it saves energy for the mother on the short term and prevents pregnancies which are likely to be unsuccessful due to inadequate nutrition.[5] However, this is rarely the desired outcome for women with anorexia nervosa, who often seek help with fertility problems.[30] This has significant implications for both treatment and research. In psychological treatment, it is important to shift the patient's perception of body fat as not something that is to be avoided at all costs, but an essential and complex organ in the human body that is required for optimal health, such as the return of menstruation.[31] The benefit of the return of menstruation goes beyond improved fertility: it signals the normalisation of sexual hormones, which have a widespread impact on the body, including bone health[32] and multiple pathways in the brain.[33–35] Given the complex functions of adipocytes in various organs of the body,[16] the metabolic effects of the normal body fat tissue should not be underestimated. Further research is needed to elucidate the mechanisms behind the link between minimum body fat mass, menstruation, bone and brain health in anorexia nervosa and to devise and test treatment elements including psychoeducation about adequate amounts of body fat.

REFERENCES

1. WHO. The ICD-10 classification of mental and behavioural disorders. Geneva: WHO; 2016.
2. Whalen R, Harrold J, Child S, et al. The health halo trend in UK television food advertising viewed by children: The rise of implicit and explicit health messaging in the promotion of unhealthy foods. Int J Environ Res Public Health 2018;15(3). doi: 10.3390/ijerph15030560
3. Hanachi M, Dicembre M, Rives-Lange C, et al. Micronutrients deficiencies in 374 severely malnourished anorexia nervosa inpatients. Nutrients 2019;11(4). doi: 10.3390/nu11040792
4. Mustelin L, Silen Y, Raevuori A, et al. The DSM-5 diagnostic criteria for anorexia nervosa may change its population prevalence and prognostic value. J Psychiatr Res 2016;77:85–91. doi: 10.1016/j.jpsychires.2016.03.003
5. Stoving RK. Mechanisms in endocrinology: Anorexia nervosa and endocrinology: A clinical update. Eur J Endocrinol 2019;180(1):R9–27. doi: 10.1530/EJE-18-0596
6. Berner LA, Brown TA, Lavender JM, et al. Neuroendocrinology of reward in anorexia nervosa and bulimia nervosa: Beyond leptin and ghrelin. Mol Cell Endocrinol 2018. doi: 10.1016/j.mce.2018.10.018
7. NICE. NICE Guidance 69. Eating disorders: Recognition and treatment. NICE; 2017. Available from: https://www.nice.org.uk/guidance/ng69
8. van den Berg E, Houtzager L, de Vos J, et al. Meta-analysis on the efficacy of psychological treatments for anorexia nervosa. Eur Eat Disord Rev 2019;27(4):331–51. doi: 10.1002/erv.2683

9. Zeeck A, Herpertz-Dahlmann B, Friederich HC, et al. Psychotherapeutic treatment for anorexia nervosa: A systematic review and network meta-analysis. Front Psychiatry 2018;9:158. doi: 10.3389/fpsyt.2018.00158
10. Khalsa SS, Portnoff LC, McCurdy-McKinnon D, et al. What happens after treatment? A systematic review of relapse, remission, and recovery in anorexia nervosa. J Eat Disord 2017;5:20. doi: 10.1186/s40337-017-0145-3
11. Bardone-Cone AM, Hunt RA, Watson HJ. An overview of conceptualizations of eating disorder recovery, recent findings, and future directions. Curr Psychiatry Rep 2018;20(9):79. doi: 10.1007/s11920-018-0932-9
12. Gaudiani JL, Brinton JT, Sabel AL, et al. Medical outcomes for adults hospitalized with severe anorexia nervosa: An analysis by age group. Int J Eat Disord 2016;49(4):378–85. doi: 10.1002/eat.22437
13. Goddard E, Hibbs R, Raenker S, et al. A multi-centre cohort study of short term outcomes of hospital treatment for anorexia nervosa in the UK. BMC Psychiatry 2013;13:287.
14. Fairburn CG, Cooper Z, Shafran R. Cognitive behaviour therapy for eating disorders: A "trans-diagnostic" theory and treatment. Behav Res Ther 2003;41(5):509–28.
15. Schmidt U, Ryan EG, Bartholdy S, et al. Two-year follow-up of the MOSAIC trial: A multicenter randomized controlled trial comparing two psychological treatments in adult outpatients with broadly defined anorexia nervosa. Int J Eat Disord 2016;49(8):793–800. doi: 10.1002/eat.22523
16. Funcke JB, Scherer PE. Beyond adiponectin and leptIn: Adipose tissue-derived mediators of inter-organ communication. J Lipid Res 2019. doi: 10.1194/jlr.R094060
17. Friedman J. The long road to leptin. J Clin Invest 2016;126(12):4727–34. doi: 10.1172/JCI91578
18. Francisco V, Pino J, Campos-Cabaleiro V, et al. Obesity, fat mass and immune system: Role for leptin. Front Physiol 2018;9:640. doi: 10.3389/fphys.2018.00640
19. Hasan TF, Hasan H. Anorexia nervosa: A unified neurological perspective. Int J Med Sci 2011;8(8):679–703. doi: 10.7150/ijms.8.679
20. Sadie-Van Gijsen H, Crowther NJ, Hough FS, et al. The interrelationship between bone and fat: From cellular see-saw to endocrine reciprocity. Cell Mol Life Sci 2013;70(13):2331–49. doi: 10.1007/s00018-012-1211-2
21. Ecklund K, Vajapeyam S, Mulkern RV, et al. Bone marrow fat content in 70 adolescent girls with anorexia nervosa: Magnetic resonance imaging and magnetic resonance spectroscopy assessment. Pediatr Radiol 2017;47(8):952–62. doi: 10.1007/s00247-017-3856-3
22. Watson HJ, Yilmaz Z, Thornton LM, et al. Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa. Nat Genet 2019 doi: 10.1038/s41588-019-0439-2
23. Yilmaz Z, Gottfredson NC, Zerwas SC, et al. Developmental premorbid body mass index trajectories of adolescents with eating disorders in a longitudinal population cohort. J Am Acad Child Adolesc Psychiatry 2019;58(2):191–99. doi: 10.1016/j.jaac.2018.11.008
24. El Ghoch M, Pourhassan M, Milanese C, et al. Changes in lean and skeletal muscle body mass in adult females with anorexia nervosa before and after weight restoration. Clin Nutr 2017;36(1):170–78. doi: 10.1016/j.clnu.2015.10.006
25. El Ghoch M, Calugi S, Milanese C, et al. Body composition in men with anorexia nervosa: Longitudinal study. Int J Eat Disord 2017;50(7):856–60. doi: 10.1002/eat.22721
26. El Ghoch M, Calugi S, Chignola E, et al. Body mass index, body fat and risk factor of relapse in anorexia nervosa. Eur J Clin Nutr 2016;70(2):194–8. doi: 10.1038/ejcn.2015.164
27. El Ghoch M, Calugi S, Chignola E, et al. Body fat and menstrual resumption in adult females with anorexia nervosa: A 1-year longitudinal study. J Hum Nutr Diet 2016;29(5):662–6. doi: 10.1111/jhn.12373
28. El Ghoch M, Pourhassan M, Milanese C, et al. Changes in lean and skeletal muscle body mass in adult females with anorexia nervosa before and after weight restoration. Clin Nutr 2015;28:28. doi: 10.1016/j.clnu.2015.10.006

29. El Ghoch M, Calugi S, Lamburghini S, et al. Anorexia nervosa and body fat distribution: A systematic review. Nutrients 2014;6(9):3895–912. doi: 10.3390/nu6093895
30. Easter A, Naumann U, Northstone K, et al. A longitudinal investigation of nutrition and dietary patterns in children of mothers with eating disorders. J Pediatr 2013;163(1):173–8.e1. doi: 10.1016/j.jpeds.2012.11.092
31. Mantzoros CS, Magkos F, Brinkoetter M, et al. Leptin in human physiology and pathophysiology. Am J Physiol Endocrinol Metab 2011; 301(4):E567–84. doi: 10.1152/ajpendo.00315. 2011
32. Misra M, Klibanski A. Bone metabolism in adolescents with anorexia nervosa. J Endocrinol Invest 2011;34(4):324–32. doi: 10.3275/7505
33. Le Moene O, Agmo A. The neuroendocrinology of sexual attraction. Front Neuroendocrinol 2018;51:46–67. doi: 10.1016/j.yfrne.2017.12.006
34. Habib P, Beyer C. Regulation of brain microglia by female gonadal steroids. J Steroid Biochem Mol Biol 2015;146:3–14. doi: 10.1016/j.jsbmb. 2014.02.018
35. Hausmann M. Why sex hormones matter for neuroscience: A very short review on sex, sex hormones, and functional brain asymmetries. J Neurosci Res 2017;95(1–2):40–9. doi: 10.1002/jnr.23857

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