Author/s:
Phillipou, A;Rossell, SL;Castle, DJ

Title:
Anorexia nervosa or starvation?

Date:
2018-12-01

Citation:
Phillipou, A., Rossell, S. L. & Castle, D. J. (2018). Anorexia nervosa or starvation?. European Journal of Neuroscience, 48 (11), pp.3317-3318. https://doi.org/10.1111/ejn.14158.

Persistent Link:
https://hdl.handle.net/11343/284526

DR. ANDREA PHILLIPOU (Orcid ID : 0000-0003-1009-6619)

Article type : Editorial

Anorexia Nervosa or Starvation?

Andrea Phillipou[a,b,c,d], Susan Lee Rossell[a,b,e], David Jonathan Castle[b,c]

[a] Centre for Mental Health, Swinburne University of Technology, Melbourne, VIC, Australia

[b] Department of Psychiatry, St Vincent's Hospital, Melbourne, VIC, Australia

[c] Department of Psychiatry, The University of Melbourne, Melbourne, VIC, Australia

[d] Department of Mental Health, The Austin Hospital, Melbourne, VIC, Australia

Corresponding author: Dr Andrea Phillipou, Centre for Mental Health, Swinburne University of Technology, PO Box 218 (H99), Hawthorn, VIC 3122, Australia. Ph: +61 3 9214 8755. e: andreaphillipou@swin.edu.au

Proposed journal section: Cognitive Neuroscience

Pages: 6; Figure:0; Tables:0; Equations:0

Word count, text: 830

Keywords: eating disorder; neurobiology; malnutrition; neurocognition; fasting

Is this related to anorexia nervosa or to starvation? Every individual conducting research in anorexia nervosa (AN) has undoubtedly asked themselves this question. AN is an incredibly difficult illness to research as it is fundamentally a mental illness but results in very serious physical consequences. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), AN is characterised by a disturbance of body image and a restriction of energy intake leading to significantly low body weight (American Psychiatric Association, 2013). A significant change in physical state (i.e. significant weight loss) is thus a core diagnostic criterion. Thus, a diagnosis of AN is dependent on an individual starving themselves to achieve a significant reduction in their body weight. Starvation results in undeniable physiological changes throughout the body, including the brain. As a consequence, essentially all research undertaken in AN, with the exception of some fields such as genetics, is influenced to some degree by the malnourished state of patients. **An additional complexity is that some people with AN also engage in binging and purging as well as other strategies to lose weight, including excessive exercise.** Disentangling whether findings are due to the illness itself, or are epiphenomena consequent upon starvation is an exceptionally difficult task. In an attempt to **control for the effects of starvation on research findings**, individuals who are weight-restored or recovered from AN are often assessed rather than acutely unwell and underweight patients. To date, this is perhaps the most widely used method to overcome this confound. However, the long-term effects of starvation on the brain are relatively unknown (Phillipou *et al.*, 2014a), leaving us essentially in the same position as assessing underweight patients.

To identify whether research findings are a result of the illness or a consequence of starvation, a control group of healthy individuals who have been deprived adequate nutrition for a sustained period of time would be required. In modern times, this would indisputably be considered unethical. However, prior to the introduction of strict ethical standards, a number of human starvation studies were undertaken. The most famous of these is the Minnesota Starvation Experiment conducted by Keys *et al.* (1950) in which 36 young males underwent partial starvation for six months. A number of physiological and psychological variables were monitored and assessed throughout this period, many of which demonstrated striking similarities to AN, including severe emotional distress and depressive symptoms, self-harm, social withdrawal, and repetitive, obsessive/perfectionistic and ritualistic behaviours relating

to food and eating. These behaviours are also often linked to serotonin depletion (Lucki, 1998), which may be expected considering an estimated 95% of serotonin is produced in the gastrointestinal tract (Kim & Camilleri, 2000), and the restriction of food consumption alters the integrity of this organ system.

A small number of more recent studies have also shed light onto the cognitive effects of *short-term fasting* in healthy individuals, including deficits in cognitive flexibility (Piech *et al.*, 2009) and attentional biases to food stimuli (Placanica *et al.*, 2002); behaviours often characteristic of AN. Changes in cognition, such as deficits in short term memory, have also been reported in groups who experience rapid weight loss such as athletes in preparation for competition (Choma *et al.*, 1998). Relatedly, the effects of *long-term fasting* and starvation are likely to significantly alter cognitive functioning in AN. Therefore, the persistence of cognitive alterations and associated behaviours may play a role in habit learning that support the maintenance of the illness.

Despite the similarities between starvation effects and AN symptomatology, starvation-related findings are often overlooked in the literature and these characteristics are frequently attributed as trait features of AN as they often continue into recovery. **It is, however, unclear whether the consequences of starvation might also be a consequence of AN.** To allow the field of AN to move forward, we need to focus our attention on disentangling the effects of the illness from that of starvation. Early human starvation studies provide a basis for this. Investigating gut-brain interactions in AN will also provide further insight into the illness, and is an emerging area of interest in the field. A greater number of rigorous and systematic retrospective and family-based studies are also required to shed light onto features of AN prior to illness onset, and consequently, identify whether they are present irrespective of starvation. Thorough investigations in atypical AN are also essential. Individuals with atypical AN meet all criteria for AN, but despite significant weight loss, are not underweight. Rigorous psychological, biological and neurobiological investigations comparing typical with atypical AN patients is critical for unravelling the effects of starvation in this illness. Furthermore, greater research into at-risk groups and individuals in the early phases of illness (with presumably only short-term starvation) is essential to enhance our understanding of the disorder. The identification of reliable and valid biomarkers for AN are critical for this purpose, but are not yet available for AN (Phillipou *et al.*, 2014b). Biomarker identification is an essential area of research that needs to be pursued in AN.

Distinguishing AN from the effects of starvation is essential to our understanding of the illness and will ultimately lead to the development of more effective treatments. Until we

are able to differentiate between AN and starvation, we cannot be confident in almost all research findings in this illness.

Acknowledgements: None

Disclosures: Prof. Castle reports grants and/or personal fees from Eli Lilly, Janssen-Cilag, Roche, Allergen, Bristol-Myer Squibb, Pfizer, Lundbeck, AstraZeneca, Hospira, Organon, Sanofi-Aventis, Wyeth and Servier, during the conduct of the study and outside the submitted work. Dr Phillipou and Prof Rossell report no conflicts of interest.

Author contributions: AP wrote the first draft of the manuscript; all authors contributed to revisions and approved the final manuscript.

References

American Psychiatric Association (2013) *Diagnostic and Statistical Manual of Mental Disorders 5*. American Psychiatric Association, Washington, DC.

Choma, C.W., Sforzo, G.A. & Keller, B.A. (1998) Impact of rapid weight loss on cognitive function in collegiate wrestlers. *Medicine and science in sports and exercise*, **30**, 746-749.

Keys, A., Brozek, J., Henschel, A., Mickelsen, O., Taylor, H.L., Simonson, E., Skinner, A.S. & Wells, S.M. (1950) *The biology of human starvation*. University of Minnesota Press, Minneapolis, MN.

Kim, D.-Y. & Camilleri, M. (2000) Serotonin: a mediator of the brain-gut connection. *The American journal of gastroenterology*, **95**, 2698.

Lucki, I. (1998) The spectrum of behaviors influenced by serotonin. *Biological psychiatry*, **44**, 151.

Phillipou, A., Rossell, S.L. & Castle, D.J. (2014a) The neurobiology of anorexia nervosa: A systematic review. *Australian and New Zealand Journal of Psychiatry*, **48**, 128-152.

Phillipou, A., Rossell, S.L., Castle, D.J., Gurvich, C. & Abel, L.A. (2014b) Square Wave Jerks and Anxiety as Distinctive Biomarkers for Anorexia Nervosa. *Investigative ophthalmology & visual science*, **55**, 8366-8370.

Piech, R.M., Hampshire, A., Owen, A.M. & Parkinson, J.A. (2009) Modulation of cognitive flexibility by hunger and desire. *Cognition and Emotion*, **23**, 528-540.

Placanica, J.L., Faunce, G.J. & Soames Job, R.F. (2002) The effect of fasting on attentional biases for food and body shape/weight words in high and low Eating Disorder Inventory scorers. *The International journal of eating disorders*, **32**, 79-90.