Dietary polyunsaturated fatty acids and anorexia nervosa: is there a link?

Dr. Agnes K Ayton
Consultant Child and Adolescent Psychiatrist, The Huntercombe Stafford Hospital

During the last 30 years, there has been an increasing interest in the general medical literature in the function of lipids and adipose tissue in humans. However, there has been little research examining the link between dietary fat intake and the symptoms and consequences of anorexia nervosa.

Dietary fats have perhaps not received attention in the eating disorder literature because humans can manufacture most fats from other macronutrients, and therefore it has been assumed that any depletion of body fat mass can be quickly restored simply by increasing the caloric intake. However, this is not so: certain polyunsaturated fatty acids (PUFAs) are essential and humans rely entirely on their diet to obtain the main precursors.

Linoleic acid (LA) and alpha-linolenic acid (LNA) are essential fatty acids (EFA). LA is the main dietary precursor of n-6 fatty acids, whilst LNA is the precursor of n-3 fatty acids. Although the minimal daily requirement has not been established [2,3], prolonged dietary deprivation of LA and LNA is incompatible with life [4]. Gross deficiencies of n-6 and n-3 PUFA have been observed in humans, induced by early attempts at total parenteral nutrition. The n-6 and n-3 fatty acids influence eicosanoid metabolism, gene expression, and intercellular cell-to-cell communication. These two classes of PUFA are metabolically and functionally distinct and their balance is important for homeostasis, normal functioning, and development. PUFAs are both essential components of the phospholipid (PL) membrane of all cells in the body, and the human brain is particularly rich in these substances.

The current western diet lacks sufficient n-3 fatty acids. Over the last hundred years, there has been a massive increase of consumption of vegetable oils and hydrogenated vegetable oils - which are rich in trans-fatty acids and n-6 PUFAs at the expense of n-3 fatty acids. The human diet until the last 100-150 years contained about 1:1 proportion of n-6: n-3 PUFAs, whilst the ratio in modern diet is about 20:1, and this may contribute to the increase of some the common diseases in developed countries [5].

There is increasing evidence of the health benefits of n-3 PUFA supplementation in a number of medical conditions, including heart disease [6,7], auto-immune disorders[8,9], cachexia [10-12]. Preliminary studies indicate that n-3 PUFA supplementation might be helpful in various psychiatric disorders, notably in severe bipolar disorder [13], treatment resistant depression (ethyl-EPA), schizophrenia and aggression [14-16]. The results in schizophrenia are inconclusive [17-20].

It is highly likely that prolonged dieting during anorexia affects PUFA reserves in the body and their availability for the brain. Current re-feeding programmes do not take into consideration the n-3 fatty acid intake (the n-6: n-3 ratio is 6:1 in artificial feeds) and it is possible that as a result of this, some patients will develop further n-3 PUFA deficiency during weight restoration. This may contribute to deteriorating mood and early relapse, both of which are very common problems after re-feeding. Fatty acid deficiencies might also contribute to the intergenerational transmission of anorexia nervosa. Although direct evidence is limited, we have some experimental data available to support this hypothesis, and we hope to carry out further research in this area.

Reference List

1. Ayton,A.K. Dietary polyunsaturated fatty acids and anorexia nervosa: Is there a link? Nutritional Neuroscience . 7, (2004).

2. Simopoulos,A.P. Omega-3 fatty acids in health and disease and in growth and development. [see comments.]. [Review] [211 refs]. Am J Clin Nutr 54, 438-463 (1991).

3. Simopoulos,A.P. Essential fatty acids in health and chronic disease. [Review] [98 refs]. Am J Clin Nutr 70, 560S-569S (1999).

4. Bjerve,K.S., Thoresen,L., Mostad,I.L. & Alme,K. Alpha-linolenic acid deficiency in man: effect of essential fatty acids on fatty acid composition. Advances in Prostaglandin, Thromboxane, & Leukotriene Research 17B, 862-865 (1987).

5. Simopoulos,A.P. Omega-3 fatty acids in health and disease and in growth and development. [see comments.]. [Review] [211 refs]. Am J Clin Nutr 54, 438-463 (1991).

6. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet 354, 447-455 (1999).

7. Durrington,P.N. et al. An omega-3 polyunsaturated fatty acid concentrate administered for one year decreased triglycerides in simvastatin treated patients with coronary heart disease and persisting hypertriglyceridaemia. Heart (British Cardiac Society) 85, 544-548 (2001).

8. Calder,P.C. Polyunsaturated fatty acids, inflammation, and immunity. [Review] [165 refs]. Lipids 36, 1007-1024 (2001).

9. Kelley,D.S. Modulation of human immune and inflammatory responses by dietary fatty acids. [Review] [51 refs]. Nutrition 17, 669-673 (2001).

10. Tisdale,M.J. & Dhesi,J.K. Inhibition of weight loss by omega-3 fatty acids in an experimental cachexia model. Cancer Research 50, 5022-5026 (1990).

11. Karmali,R.A. Historical perspective and potential use of n-3 fatty acids in therapy of cancer cachexia. [Review] [19 refs]. Nutrition 12, S2-S4 (1996).

12. Wigmore,S.J. et al. The effect of polyunsaturated fatty acids on the progress of cachexia in patients with pancreatic cancer. Nutrition 12, S27-S30 (1996).

13. Stoll,A.L. et al. Omega 3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. [see comments.]. Archives of General Psychiatry 56, 407-412 (1999).

14. Hibbeln,J.R., Umhau,J.C., George,D.T. & Salem,N., Jr. Do plasma polyunsaturates predict hostility and depression?. [Review] [69 refs]. World Review of Nutrition & Dietetics 82, 175-186 (1997).

15. Hibbeln,J.R. et al. A replication study of violent and nonviolent subjects: cerebrospinal fluid metabolites of serotonin and dopamine are predicted by plasma essential fatty acids. Biological Psychiatry 44, 243-249 (1998).

16. Buydens-Branch, Branchey,M., McMakin,D.L. & Hibbeln,J.R. (2003) Polyunsaturated fatty acid status and aggression in cocaine addicts. Drug and Alcohol Dependence .

17. Puri,B.K. & Richardson,A.J. Sustained remission of positive and negative symptoms of schizophrenia following treatment with eicosapentaenoic acid. Arch Gen Psychiatry 55, 188-189 (1998).

18. Peet,M., Horrobin,D.F. & Study Group,E.-E.M. A dose-ranging exploratory study of the effects of ethyl-eicosapentaenoate in patients with persistent schizophrenic symptoms. Journal of Psychiatric Research 36, 7-18 (2002).

19. Fenton,W.S., Dickerson,F., Boronow,J., Hibbeln,J.R. & Knable, M. A placebo-controlled trial of omega-3 fatty acid (ethyl eicosapentaenoic acid) supplementation for residual symptoms and cognitive impairment in schizophrenia. Am J Psychiatry 158, 2071-2074 (2001).

20. Fenton,W.S., Hibbeln,J. & Knable,M. Essential fatty acids, lipid membrane abnormalities, and the diagnosis and treatment of schizophrenia. [Review] [126 refs]. Biological Psychiatry 47, 8-21 (2000).

Insight

Lynn McLeish
Director of Specialised Services, The Huntercombe Hospitals

Welcome to this, the first edition of Insight. As one of the leading specialists, we are keen to inform and update you on issues relating to the treatment of patients with mental health problems. In this first issue, you can find articles by experts in eating disorders, all of whom work for The Huntercombe Hospitals. Future editions will focus on other problems affecting adolescents. Should any of the articles prompt questions, do feel free to contact the authors, or any of the other members of the team. Details of all our hospitals and centres are on the back page.

A Psychotherapeutic approach

Dr. David Tait
Medical Director, The Huntercombe Edinburgh Hospital

Psychotherapy research is notoriously difficult methodologically, given the complex nature both of problems and treatment. That being said, there is some evidence of effectiveness of specifically tailored cognitive behavioural therapy in bulimia nervosa and for family work with younger patients suffering from anorexia nervosa.

Things are much more complex with an inpatient population. The primary diagnosis is almost always anorexia nervosa, but secondary diagnoses are the rule, rather than the exception, depression, obsessive-compulsive disorder and substance misuse being commonplace. This is in addition to prominent complicating symptoms and behaviours such as low self-esteem or repeated self-harm. Most patients will have long histories and failed treatment in other settings. Psychological problems will commonly be seen as (partially) causal, and in virtually all cases will be consequential upon the illness.

It is in this setting that evidence-based medicine must be balanced against "practice-based evidence". Management includes specific treatments for the eating disorder itself (e.g. addressing distorted body image or purging behaviour), for associated symptoms (e.g. low self-esteem), for co-morbid problems and finally for the pervasive psychological difficulties involved. It is interesting that in the psychotherapy literature, the word "rehabilitation" is sometimes used for longer term, more fundamental psychotherapies. This sits comfortably with the use of the term rehabilitation in the general psychiatric sense. Our eating disorder inpatients have been out of mainstream domestic, occupational, educational and recreational life and require an imaginative, but still traditional, rehabilitative approach; alongside this they require psychotherapeutic rehabilitation.

The psychotherapeutic task is twofold – creating a therapeutic milieu within the hospital and providing individualised treatments for each patient. At The Huntercombe Edinburgh Hospital we are well placed to provide this with one consultant (the author) on the specialist register for both general psychiatry and psychotherapy, and the other (John Duncan) a child and adolescent psychiatrist whose practice has been family orientated throughout his career. We have 4.5 whole time equivalent posts in psychotherapeutic treatments (two full timers and four part timers in post, plus one vacancy at present), a number of these individuals are dual trained, this training encompassing psychoanalytic, group analytic gestalt and integrative psychotherapies, clinical and counselling psychology, cognitive behavioural and cognitive analytic therapy, motivational therapy, transactional analysis and art therapy. In addition, a number of these staff are very experienced in family work. As important as these trainings are, the maturity and eclecticism of the team ensures that all psychotherapeutic needs can be met.

Having focused upon this aspect of our treatment programme, I should of course underline that this is embedded in an infrastructure including two staff grade psychiatrists, a full complement of registered mental health and sick children's nurses, a dietician who also manages our catering service, an occupational therapist and activities co-ordinator, and two teachers for our younger patients. In consequence, we are able to offer a truly comprehensive treatment programme.

INSIDE:

How we provide an eating disorders service for the most severely ill patients

Dr. Mark Tattersall
Medical Director,
The Huntercombe Maidenhead Hospital

Imagine, if you will, the most taxing and worrying patients with eating disorders. Severely malnourished adolescents unable to accept that they are ill, and totally refusing to eat or even drink; young people so enmeshed in a pattern of self-induced vomiting that they risk fatal cardiac arrhythmias every day; abused teenagers who have learnt to control and cope with their tangled emotions and traumatic memories by both starvation and self-harming, regardless of the risks of both; inpatients who have exceeded the resources of their treating team, overwhelming all around them with uncontainable anxieties, and putting themselves and their peers at risk.

Other people's nightmare clinical scenarios like these, and more, are our everyday work, and a challenge that we relish. How?

The key is the combination of having sufficient resources to do the job, and the confidence borne of training and experience that a way can and will be found to work with the most "ill", "damaged" and "stuck" young people. Through both supporting them to safely regain physical health and helping them (and their families) to engage in a range of therapies, we can enable each one to find their own individual and effective path to a healthier and more fruitful future. Indeed, we have often found that the most severely ill patients (especially those who have had life threatening complications) often, in time, make the fullest recoveries.

At The Huntercombe Maidenhead Hospital we have developed two age-stratified specialist eating disorder units, which between them provide inpatient and (where indicated and agreed) transitional / follow-on outpatient treatment for young people aged 13 to 25 with severe eating disorders. We have developed our service to work in support of local NHS teams and regional inpatient units to provide intensive and highly specialised treatment for those most severely ill patients for whom attempts to treat within the usual range of services have failed, or would be unsafe.

We accept referrals from the patient's NHS Consultant and work with them to develop a care plan that helps the patient reach a stage in their recovery where they can effectively complete their recovery back in the community. Our full team assessment may provide the referrer with the advice and support they need to be able to continue to manage the patient, or may form the basis for an agreement to provide a period of intensive inpatient treatment. Although our consultant takes full responsibility for ensuring the provision of all aspects of the patient's specialist treatment, the development of the patient's care plan (and especially discharge planning) always involves the patient, parents/carers, the referrer, the GP and the Primary Care Trust. In addition to the regular CPA meetings where these issues are discussed, the Consultant is always contactable by all parties to ensure that we continue to work together for the benefit of the patient.

NICE guidelines highlight the importance of multidisciplinary working in treating anorexia nervosa, and we extend this principle beyond the walls of the unit to include all members of the patient's team (and particularly parents/carers) in order to provide optimally effective and safe treatment.

We are able to work with very underweight patients because we not only provide effective psychological support for re-feeding, but also can safely manage the medical risks of re-feeding in such patients. We have the skills and resources to provide naso-gastric feeding on the unit on those occasions when this is indicated, and on rare occasions to arrange for a PEG feeding gastrostomy as a life saving measure, or for temporary transfer of highly suicidal or otherwise severely disturbed patients to our on site specialist adolescent intensive care units. When all parties know that the treatment team has the ability to safely and effectively manage the full range of possible risks, this is immensely reassuring and containing and lays the foundations for the psychological work of recovery.

In addition to our specialist nurses and psychiatrists, our team includes a senior clinical psychologist, counselling psychologists, family

therapists, an art therapist, physiotherapists, a dietician, social worker and an activities coordinator.

The breadth and experience of the team allows us to effectively address the range of co-morbidities (such as obsessive compulsive disorder, depression, complex post-traumatic stress disorder and chronic fatigue syndrome) that are commonly reasons why a person with an eating disorder might not respond to more "first line" treatment. We also work closely with our in house education team to provide on site education up to GCSE level, as well as assistance for AS and A2 studies, and have a full range of indoor and outdoor recreation and sports facilities to support normal healthy adolescent interests and development. Meanwhile, our well resourced research team is hard at work helping us to evaluate and further refine our treatment interventions.

So the answer is simple really – cover all the angles, keep all the balls in the air (a comprehensive and coordinated team comes in handy here), and keep hope alive!

Latest news from around The Huntercombe Hospitals

- At The Huntercombe Maidenhead Hospital, recent senior appointments are: Dr. Sharon Davies as a Consultant in Child & Adolescent Psychiatry and Peter Morris as a Clinical Psychologist.
- Shelagh Wright from The Huntercombe Maidenhead has been awarded a Doctorate in Systemic Psychotherapy.
- Dr. Frank Zaw from The Huntercombe Stafford Hospital presented 3 papers at the Edinburgh meeting of the Royal College of Psychiatrists.
- The Huntercombe Roehampton Hospital, which opened in Spring 2004, is a finalist for a healthcare building design award.

Early onset eating disorders research at The Huntercombe Hospitals

by Kate Willoughby, Harriet McIlwham and Bryan Lask

Professor Bryan Lask
Medical Advisor,
The Huntercombe Hospitals

The Huntercombe Hospitals, in conjunction with St Georges Hospital Medical School, under the direction of Professor Bryan Lask, have an active clinical research programme which attempts to further advance the understanding of eating disorders in the younger population. The Huntercombe Maidenhead Hospital has been research active since the service was set up in 1994 and has recently provided a springboard for the development of research within the two newly established services at The Huntercombe Edinburgh and Huntercombe Stafford Hospitals.

Studies include aetiology, assessment, treatment, co-morbidity, course and factors that influence outcome. Some of the more significant ones are outlined below:

i) Neurobiology and neuropsychology of anorexia nervosa: this series of studies has demonstrated a complex set of abnormal brain functioning in AN, with specific abnormalities within the limbic system, further supporting the hypothesis of neuronal circuit abnormality. The findings appear to be primary rather than secondary phenomena in that they do not reverse with weight restoration. Further studies are being planned using neuro-cognitive tasks conducted alongside fMRI.

ii) A series of studies into season of birth in early onset anorexia nervosa has shown a bias toward spring births, in both northern and southern hemispheres. We are now exploring the hypothesis that this bias is as a result of impaired maternal fertility during the winter months due to restrictive eating and lower weight.

iii) A study of primary care consultations in the 5 years prior to the diagnosis of anorexia nervosa being made, revealed that its onset can be predicted on the basis of just one consultation regarding weight or shape concerns.

iv) A number of assessment instruments commonly used in adults with eating disorders have been adapted and validated for the younger population. These include the PCAN, the SEDS and the SAWBS.

v) For many years we have been investigating the use of pelvic ultrasound as a means of assessing pelvic organ maturity in anorexia nervosa. This has shown that a BMI of less than 20 is inadequate to guarantee restoration of normal pelvic organ functioning. We have now developed an algorithm to aid clinicians in the use of pelvic ultrasound.

vi) Investigation of co-morbidity has shown a high prevalence of obsessive-compulsive disorder, indicating the need for careful attention to this commonly undiagnosed co-morbid disorder.

vii) The process of recovery, and its implications for treatment, is not often considered or empirically explored. Willoughby, as part of her PhD, is investigating systematically the stages of recovery previously described by Lask and Bryant-Waugh.

viii) The outcome for early onset anorexia nervosa is unsatisfactory. In consequence we are investigating the prognostic factors for outcome so that more detailed therapeutic attention can be paid to those associated with a poorer prognosis.

ix) Twins with anorexia nervosa can tell us much about the relative roles of genetic and environmental factors. Wright has recently completed a doctorate investigating the significance of shared and non-shared environments.

x) The role of polyunsaturated fatty acids in anorexia nervosa has been investigated by Ayton (see over) and a treatment trial is planned.

References for work published between 2000 and 2005

Lask B., Bryant-Waugh, R., Wright, F., Campbell, M., Willoughby, K., & Waller, G. (2005) General practitioner consultations indicating high risk for early-onset anorexia nervosa. (In press- International Journal of Eating Disorders).

Lask, B., Gordon, I., Christie, D., Frampton, I., & Watkins B.(2005) Neuroimaging in early Onset AN (In press- International Journal of Eating Disorders)

Willoughby, K., Bowen, R., Parvathy P., Lee, E. L. & Lask, B. (2005) Pattern of Birth in Early Onset Anorexia Nervosa: An Equatorial Study. (In press- International Journal of Eating Disorders).

Serpell, L., Neiderman, M., Bird, E., Lask, B. et al. (2005) Shape- and weight-based self esteem in children and adolescents with eating disorders. (In press Eating Behaviours)

Mason, H., Key, A., Allan, R. & Lask, B. An algorithm for the use of pelvic ultrasound in AN. (Submitted)

Serpell, L., Hirani, V., Willoughby K., Niederman, M. & Lask, B. Personality or pathology?: Obsessive-compulsive symptoms in children and adolescents with anorexia nervosa. (Submitted)

Willoughby K et al (2005) Season of birth in early onset anorexia nervosa in an equatorial region. (In press International J. of Eating Disorders)

Serpell L, Neiderman M, Haworth E, Emanuelli F, Lask B (2003) The use of the pros and cons of anorexia nervosa (P-CAN) scale with children and adolescents. J. of Psychosomatic Research, 5:567-571

Chowdhury U, Gordon I, Lask B, Christie D, Wigley K, Watkins B (2003) Early onset anorexia nervosa: evidence of limbic system imbalance. International Journal of Eating Disorders 33:388-396

Waller G, Watkins B, Potterton C, Neiderman M, Sellings J, Willoughby K, Lask B (2002). Pattern of birth in adults with anorexia nervosa J. of Nervous and Mental Disease

Key A, Mason H, Allen R, Lask B (2002) Restoration of ovarian and uterine maturity in adolescents with anorexia nervosa. International Journal of Eating Disorders, 32: 319-325.

Campbell M, Lawrence B, Neiderman M, Serpell L, Lask B (2002). Validation of the Sterling Eating Disorders Scale in an adolescent population. Eating Behaviours, 3, 285-293

Serpell L, Livingstone A, Neiderman M, Lask B . (2002) Anorexia nervosa: obsessive-compulsive disorder, obsessive-compulsive personality disorder, or neither? Clinical Psychology Review 24: 647-669

Watkins B, Willoughby K, Waller G, Serpell L, Lask B.(2002) Pattern of birth in anorexia nervosa 1: early onset cases in the United Kingdom. International J. of Eating Disorders 32 (1) 11-17

Willoughby K, Watkins B, Beumont P, Maguire S, Lask B and Waller G (2002) Pattern of birth in early onset anorexia nervosa 11: A comparison of Northern and Southern hemispheres. International J. of Eating Disorders 32 (1) 18-23

Chowdhury, U and Lask, B. (2001). Clinical implications of brain imaging in Eating Disorders. Psychiatric Clinics of N. America: 24, 227-234

Neiderman, M., Richardson, J., Farley, A. and Lask, B. (2001). Naso-gastric feeding in early-onset eating disorders. International Journal of Eating Disorders. 29: 441-448.

Chowdhury, U and Lask, B (2000) Neurological Correlates of Eating Disorders. European Eating Disorders Review Vol 8; 2:126-133.

Neiderman, M., Zardy, M., Tattersall, M. and Lask, B. (2000). Enteric feeding in early-onset anorexia nervosa. International Journal of Eating Disorders 28: 470-5

Lask B and Bryant-Waugh R (2000) Anorexia Nervosa and Related Eating Disorders in Childhood and Adolescence Psychology Press, UK

We are most grateful to the Health Foundation for financial support and to many other colleagues and institutions with whom we have collaborated over the years.