**Sir:** As a practising psychiatrist and psychoanalyst, I welcomed Hinshelwood's (1999) editorial which highlights the problem we face in helping difficult patients. Although I agree with his description of the defensive use of 'scientific psychiatry' in these areas, I am concerned he has fallen into the trap that he wished to avoid, namely, an overtly simple split between objective science and subjectivity.

The problem, I think, is to equate positivist scientific research with a scientific approach that could simply be called 'the search for truth' and which is central to all clinical work. What I think is missing from Hinshelwood's argument is the centrality of the problem that we all have of inquiry into the truth. This is as important in psychotherapy as it is in empirical science. Whether we are carrying out a research project looking into epidemiology, or assessing a patient in order to decide about diagnosis and treatment, or listening to a patient in a psychotherapy session in order to decide what would be the most helpful comment to make, we are involved in a process of inquiry that involves gathering information and making judgements. I think we have considerable resistance to this process in terms of learning the truth and making critical judgements.

Learning the truth not only makes us face what may be unpleasant and potentially painful but also makes us face our limitations in terms of our knowledge and what we can do to help our patients.

Making judgements involves taking authority and is often confused with being judgemental. I believe that an overly subjective approach that eschews inquiry, as much as an overly objective scientific approach, are both ways of avoiding this and are equally dangerous. I am sceptical that often objective empirical research, which now dominates psychiatry, is not actually about discovering the truth, but is a means of confirming convictions of what is already believed to be the truth. I think Hinshelwood is right to point out how this approach is often used to avoid the disturbance of our patients but he has not stressed the emotional difficulties faced in truth-seeking research nor the dangers of over-subjectivity.

**Hinshelwood, R. D. (1999)** The difficult patient. The role of 'scientific psychiatry' in understanding patients with chronic schizophrenia or severe personality disorder. *British Journal of Psychiatry*, **174**, 187–190.

**D. Simpson** Tavistock Clinic, 120 Belsize Lane, London NW3 5BA

## Lipids and schizophrenia

**Sir:** I was pleased to see the potential importance of lipid metabolism in schizophrenia recognised by an editorial (Walker *et al*, 1999). It is unfortunate, however, that the review of the literature is highly selective and omits many recent findings, possibly because of the delay between first submission and publication. The main omissions are first, there is now substantial evidence for two abnormalities in phospholipid metabolism in schizophrenia (Horrobin, 1998, 1999). One is an increased rate of breakdown of phospholipids. The other is a reduced rate of incorporation of highly unsaturated fatty acids (HUFAs) into phospholipids.

Second, a phospholipase $A_2$ ($PLA_2$) and specifically a calcium-independent $PLA_2$, is a strong candidate for the protein involved in increased phospholipid breakdown (Ross *et al*, 1997). One of the fatty acid coenzyme A ligases (FACLs), and specifically FACL-4, is a strong candidate for the defect in incorporating HUFAs into phospholipids (Piccini *et al*, 1998). The FACL enzymes rapidly remove free HUFAs from the cytoplasm. When they are defective, increased free HUFA levels lead to excess HUFA oxidation.

Third, the simultaneous presence of a $PLA_2$ and an FACL abnormality will have important consequences because these are two key enzymes involved in the signal transduction processes following activation of various receptors, including $D_2$ and 5-$HT_2$ receptors. Activation of those receptors leads to a change in G-protein configuration and $PLA_2$ activation. $PLA_2$ activation leads to the formation of two highly active signal transduction molecules, a lysophospholipid and a free HUFA. This activation process must be rapidly terminated. This is achieved by the formation of HUFA–coenzyme A under the influence of FACL, and the re-formation of a stable phospholipid by linking the HUFA back to the lysophospholipid. The simultaneous presence of a $PLA_2$ and an FACL abnormality will lead to defective incorporation of HUFAs into cell signalling compartments and increased oxidation of HUFAs.

Fourth, an overactivity of $PLA_2$ would explain why $D_2$ and 5-$HT_2$ blockers are particularly effective in schizophrenia, even though in unmedicated patients abnormalities in dopamine or serotonin metabolism or abnormalities in their receptors have been hard to find or replicate. Since $D_2$ and 5-$HT_2$ receptor occupation provide part of the drive to $PLA_2$ activation (Vial & Piomelli, 1995), blockade of these receptors will decrease $PLA_2$ activity but not normalise it if the abnormality is actually at the signal transduction level. This may help to explain why the average effect sizes of both old and new neuroleptics are always less than 30%.

**Horrobin, D. F. (1998)** The membrane phospholipid hypothesis as a biochemical basis for the neurodevelopmental concept of schizophrenia. *Schizophrenia Research*, **30**, 193–208.

__ **(1999)** Phospholipid metabolism and schizophrenia. *Schizophrenia Research*, **36**, 105–106.

**Piccini, M., Vitelli, F., Bruttini, M., et al (1998)** FACL4, a new gene encoding long-chain acyl-CoA synthetase 4, is deleted in a family with Alport syndrome, elliptocytosis, and mental retardation. *Genomics*, **47**, 350–358.

**Ross, B. M., Hudson, C., Erlich, J., et al (1997)** Increased phospholipid breakdown in schizophrenia – evidence for the involvement of a calcium-independent phospholipase A(2). *Archives of General Psychiatry*, **54**, 487–494.

**Vial, D. & Piomelli, D. (1995)** Dopamine $D_2$-receptors potentiate arachidonate release via activation of cytosolic, arachidonate-specific phospholipase $A_2$. *Journal of Neurochemistry*, **64**, 2765–2772.

**Walker, N. P., Fox, H. C. & Walley, L. J. (1999)** Lipids and schizophrenia. *British Journal of Psychiatry*, **174**, 101–104.

**D. F. Horrobin** Laxdale Research, Kings Park House, Laurelhill Business Park, Stirling FK7 9JQ

**Sir:** The recent editorial on lipid system abnormalities in schizophrenia in the *Journal* reflects the tremendous progress that is taking place on the biological frontiers in schizophrenia research (Walker *et al*, 1999), with the possibility that dietary regulation of polyunsaturated fatty acids (PUFAs) and the introduction of the so-called 'nutripharms' may herald a new chapter in the prevention of schizophrenia. However, there is evidence that the lipid dysfunction might not be specific to schizophrenia and may be present in other psychiatric disorders, notably depression.

Smith (1991) was the first person to hypothesise that an abnormal fatty acid composition may be related to the immune inflammatory pathophysiology of major depression. In another study, Finkel *et al* (1996) found that paroxetine, a selective serotonin reuptake inhibitor, acts by inhibiting the synthesis of nitric oxide, a free-radical believed to damage lipids and nucleic acids responsible for schizophrenia. This raises the intriguing possibility that

depressive disorder might be associated with free-radical damage and subsequent lipid system abnormalities.

Maes *et al* (1996) found a significant decrease in the ω3 fractions in cholesteryl esters in patients with major depression compared with minor depression or healthy controls. They also reported a significantly increased ratio of arachidonic acid to eicosapentaenoic acid in both cholesteryl esters and phospholipids. Peet *et al* (1998) found depleted total ω3 PUFA and docosahexaenoic acid in the red blood cell membrane of patients with depression. They have argued that the changes in serotonin receptor number and function caused by changes in PUFA provide the theoretical rationale connecting fatty acids with current neurotransmitter and receptor theories of depression. The possibility of dietary supplementation of fatty acids has not received enough attention in clinical trials of depression, although there are anecdotal reports of their efficacy in stress-induced aggressive behaviour (Hamazaki *et al*, 1996).

Hence, advances in lipid neurochemistry may prove useful not only in understanding schizophrenia, but also in understanding and potentially treating other psychiatric diseases including depressive disorders.

**Finkel, M. S., Thode, F. L., Pollock, B. J., *et al* (1996)** Paroxetine: a novel nitric oxide synthetase inhibitor. *Psychopharmacology Bulletin*, **32**, 653–658.

**Hamazaki, T, Sawazaki, S., Itomura, M., *et al* (1996)** The effect of docosahexaenoic acid on aggression in young adults, *Journal of Clinical Investigation*, **97**, 1129–1134.

**Maes, M., Smith, R., Christophe, A., *et al* (1996)** Fatty acid composition in major depression: Decreased ω3 fractions in cholesteryl esters and increased C 20: 4ω6/C20: 5ω3 ratio in cholesteryl esters and phospholipids. *Journal of Affective Disorders*, **38**, 35–46.

**Peet, M., Murphy, B., Shay, J., *et al* (1998)** Depletion of omega-3 fatty acid levels in red blood cell membrane of depressive patients. *Biological Psychiatry*, **43**, 315–319.

**Smith, R. S. (1991)** The macrophage theory of depression. *Medical Hypothesis*, **35**, 298–306.

**Walker, N. P., Fox, H. C. & Whalley, L. J. (1999)** Lipids and schizophrenia. *British Journal of Psychiatry*, **174**, 101–104.

**S. Swain** Department of Neurochemistry, Institute of Human Behaviour & Allied Sciences (IHBAS), Shahdara, Delhi 110095, India

**C. Pradhan** Department of Psychiatry, Institute of Human Behaviour & Allied Sciences (IHBAS), Shahdara, Delhi 110095, India

## Family functioning and adolescent anorexia nervosa

**Sir:** We read with interest the article on difficulties in family functioning and adolescent anorexia nervosa by Gowers & North (1999). This is an important area of research and we applaud the authors for a data-based publication in the *Journal*. We would, however, like to offer an alternative interpretation of their findings.

There were no significant associations between global ratings of family functioning by clinician, parent and patient and severity of anorexia nervosa; however, the authors conclude that there are some associations with separate sub-scales of family functioning. It is important first to highlight that these correlations are very small. The patients' opinion that family difficulties, such as resolving problems, increase with their increasing weight or sexual activity, is not an unexpected finding. Most patients with anorexia experience a re-emergence of feelings, particularly those of a conflictual nature, as their weight increases. This is particularly evident around sexual feelings, with which a significant proportion of adolescents with anorexia struggle. The experience of a decrease in difficult feelings with weight loss reinforces the usefulness of anorexia as a defence. Their heightened awareness of family difficulties with weight increase and clinical recovery is then to be expected.

The authors report no correlation between change in family functioning and clinical change as defined by the Morgan–Russell scale (1988). They have not given the range of change scores on their measure of family functioning, or the standard deviation. These would have facilitated the reader's assessment of the findings. The authors previously reported family functioning as predicting outcome of the anorexic illness at one year. That observation and their current finding of minimal change in family functioning during treatment cannot be offered as evidence for or against family dynamics as contributory factors in the aetiology of anorexia. We suggest that it would be more beneficial to contrast engagement or ability to effectively use therapy with family functioning. Anorexia is not caused by disturbed family dynamics; severity and aetiology of the illness is multi-factorial. However, the capacity of a family to use a treatment may be severely diminished by their own internal and difficult dynamics. The Family Assessment Device may merely be a measure of engagement which, in turn, will impact on outcome of an anorexic illness.

**Gowers, S. & North, C. (1999)** Difficulties in family functioning and adolescent anorexia nervosa. *British Journal of Psychiatry*, **174**, 63–66.

**Morgan, H. G. & Hayward, A. E. (1988)** Clinical assessment of anorexia nervosa. The Morgan–Russell outcome assessment schedule. *British Journal of Psychiatry*, **152**, 367–371.

**C. Dare** Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF

**A. Key** St George's Hospital Medical School, Cranmer Terrace, Tooting, London SW17 0RE

**Authors' reply:** We are grateful to Drs Dare and Key for their interest in and comments on our paper. They are right to draw attention to the limitations of our findings and to put the role of family difficulties in perspective alongside other variables in the multi-factorial aetiology of anorexia nervosa.

However, we wish to take issue with two of their points. First, although we agree with Dare & Key that anorexia nervosa can be interpreted as a defensive strategy against difficult feelings, this view is not universally held and, where it is, it is usually construed as an individual defence, rather than serving to reduce difficulties within the family. We contend that this is a new finding.

Second, and more importantly, the assertion that family dynamics do not cause anorexia nervosa is surely unhelpful. Although in our series, our clinical experience led us to believe that the families were without exception caring, conscientious and determined to be good families, surely family life has to be considered one of the major influences on adolescent development. If family factors can contribute to positive aspects of development like resilience, confidence, educational success and the ability to form satisfactory interpersonal relationships, then surely they can play a part in the development of negative ones. We suggest that the following features, impacting on family functioning, may, among others, be very likely to contribute to the development of eating disorders: parental disharmony and separation; parental eating disorders; death and severe illness in first-degree relatives; emotional, physical and sexual abuse; and delinquency and unwanted pregnancies in siblings and their perceived affects on family life.