One-carbon metabolism and depression

Kim et al concluded that lower levels of folate and vitamin B12 and raised homocysteine may be risk factors for late-life depression.1 We propose to include polyunsaturated fatty acids (PUFAs) in future studies that will test the potential role of one-carbon metabolism in the aetiology and persistence of depression, for several reasons. First, because one-carbon metabolism is intimately linked with PUFA metabolism.2 The methionine–homocysteine cycle produces methyl groups for the synthesis of phosphatidycholine from phosphatidylethanolamine catalysed by phosphatidylethanolamine methyltransferase. Phosphatidylcholine is critical for the delivery of important PUFAs such as docosahexaenoic acid (DHA; C22:6n-3) from the liver to the plasma and distribution to peripheral tissues. The phosphatidylcholine/phosphatidylethanolamine ratio also modulates the activity of Delta-5 and Delta-6 desaturases involved in n-3 and n-6 PUFA synthesis. Moreover, plasma homocysteine was significantly inversely correlated with DHA, total n-3 PUFAs and the n-3/n-6 PUFA ratio in healthy males.3 Second, these findings are relevant for psychiatry, as PUFAs – particularly DHA and arachidonic acid – are key ‘building stones’ that are required for healthy functioning of nerve and brain cells. In patients with recurrent depression, a decrease in n-3 PUFAs in erythrocyte membranes was found together with a significant positive association between the sum of plasma n-6 PUFAs and homocysteine.4 There is also increasing evidence from cross-sectional studies and randomised controlled trials supporting the notion that an impaired PUFA metabolism is directly linked to the onset of depression.5,6 Third, both an impaired one-carbon and an impaired PUFA metabolism might explain the positive associations between depression and metabolic syndrome (a cluster of risk factors for cardiovascular disease). Patients with depression are at risk for all components of metabolic syndrome. Interestingly, metabolic syndrome is associated with a rise in plasma homocysteine levels and a decrease in DHA in plasma and cell membranes. Based on these findings, our opinion is that for a proper understanding of underlying mechanisms linking one-carbon metabolism and depression, homocysteine, folate and B-vitamins should be measured in conjunction with dietary and laboratory analyses of PUFAs.

References
patterns of remission and relapse. However, data in their Table 1 indicates that more patients who received CBT relapsed than those who received treatment as usual (TAU) (CBT 60/122, TAU 41/119 for all the patients randomised to CBT or TAU). A statistical analysis (logistic model) for the proportion of relapses reveals a significant reduced relapse frequency for TAU.

The differences remain significant (P=0.0153) when only patients in the no-carer pathway are considered (CBT 53/97, TAU 34/92), but there are no differences for those in the carer pathway (CBT 7/25, TAU 7/27), although here the numbers are small.

It is possible that differences in gender and age distribution between the CBT and TAU arms of the trial, or even differences between centres, could have led to different results in the statistical analyses performed by the authors. However, randomisation should have minimised such differences and the authors make no mention of them in the paper.

Hence, on the basis of the results reported, CBT appears to have a detrimental effect on relapse in non-affective psychosis.


The published relapse rates after full remission and from full/partial remission in the no-carer pathway were 35.4% and 37% respectively for TAU and 46.8% and 54.6% respectively for CBT; in the carer pathways they were 21.4% and 25.9% for TAU, 27.3% and 28% for CBT, 22.2% and 20.8% for family intervention. The relapse rates point towards a significant increased risk of harm or hazard needs to have been discussed in greater detail.

With respect to the point raised by Marlowe on the effects of having a carer on a psychological intervention, we are of course very aware of the Hogarty et al study,4,5 which we also discuss. It reported mixed findings. Our point here concerned the apparently beneficial effect of having a carer on CBT, which has not been examined before.
