in the mesolimbic or mesocortical tracts, leading to an improvement in tardive psychosis.

On the other hand, clozapine, in comparison with typical antipsychotics, may not be more efficacious for new-onset schizophrenia because these patients have not been medicated previously and do not have dopaminergic upregulation that can be reversed.

Although this explanation may not be the whole story (for example, clozapine probably also has direct therapeutic effects through the D_2 or other receptors), it is a parsimonious interpretation of these data, and it suggests ideas that can be tested empirically.

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DAVID E. ROSS, M.D.
Midlothian, Va.

Schizophrenia, Syndrome X, and Omega-3 Fatty Acids

TO THE EDITOR: In an interesting study, Martina C.M. Ryan, M.B., M.R.C.Psych., et al. (1) found an increased prevalence of impaired glucose tolerance and insulin resistance in patients with drug-naive, first-episode schizophrenia in relation to healthy comparison subjects. This finding is in line with the results of a recent review showing that features of the metabolic syndrome X are more common in subjects with schizophrenia than in the general population (2). Dr. Ryan and colleagues discussed the influence of diet (1), but we believe that they omitted the possible role of polyunsaturated fatty acids of the omega-3 and omega-6 series, in particular, eicosapentaenoic acid and arachidonic acid. Substantial evidence suggests that impaired polyunsaturated fatty acid metabolism is related to both schizophrenia and the metabolic syndrome X. In recent reviews, low consumption of omega-3 polyunsaturated fatty acid was concluded to be associated with hypertriglyceridemia, cardiovascular disease, and probably also to insulin resistance and type 2 diabetes (3–5). Of interest, lowered omega-3 polyunsaturated fatty acid levels have also been reported in the erythrocytes of drug-naive psychotic patients (6) and in medicated young schizophrenic patients in comparison with normal comparison subjects (7). Furthermore, placebo-controlled trials have found eicosapentaenoic acid to be effective in schizophrenia, depression, and borderline personality disorder (8–10).

We believe that randomized, controlled trials are warranted to test whether supplementation with long-chain omega-3 polyunsaturated fatty acid, such as eicosapentaenoic acid, can improve the symptoms of schizophrenia and prevent the development of features of the metabolic syndrome X in subjects with schizophrenia.

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FRANÇOIS POUWER, PH.D.
RITSAERT LIEVERSE, M.D., M.SC.
MICHAELA DIAMANT, M.D., PH.D.
JOHANNA ASSIES, M.D., PH.D.
Fatty Acids in Diabetes, Depression, and Schizophrenia Study Group
Amsterdam, the Netherlands

Aripiprazole for Acute Bipolar Mania

TO THE EDITOR: The double-blind, randomized, placebo-controlled trial of Paul E. Keck, Jr., M.D., et al. (1) suggests that aripiprazole is effective and safe for acute bipolar episodes—mania and mixed. We consider that careful scrutiny of the methodology and the results of this study are worthwhile before integrating the study results into clinical practice.

The study incorporated patients whose mania was below 4 weeks' duration and excluded those with prior nonresponse to clozapine. Although the authors did not use a duration criterion for mixed affective episode, considering the unique pharmacodynamic properties of aripiprazole, it is unclear why such an exclusion of patients with severe and refractory mania was considered. In this study (1), there seems to be less uniformity in assessing the severity of psychopathology. While manic symptoms were quantified with the 11-item Young Mania Rating Scale (2), the measurement of severity of