

A Correction

In their article, Tohen et al¹ attribute to me the suggestion that the benefits of placebo have similarities with the benefits of psychotherapy; they then quote me as saying that both provide “expectation of improvement, support, and mobilization of hope.”

Although I heartily endorse that suggestion, it is not mine. As I make clear in the article that they cite,² Jerome Frank made that suggestion.³ Of less concern to me, the statement “quoted” from my article,² which I also endorse, is not actually in there.

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1. Tohen M, Jacobs TG, Grundy SL, McElroy SL, Banov MC, Janicak PG, Sanger T, Risser R, Zhang F, Toma V, Francis J, Tollefson GD, Breier A, for the Olanzapine HGGW Study Group. Efficacy of olanzapine in acute bipolar mania: a double-blind, placebo-controlled study. *Arch Gen Psychiatry*. 2000;47:841-849.
2. Brown WA. Placebo as a treatment for depression. *Neuropsychopharmacology*. 1994; 10:265-269.
3. Frank JD, Frank JB. *Persuasion and Healing: A Comparative Study of Psychotherapy*. Baltimore, Md: The Johns Hopkins University Press; 1991.

In reply

We thank Dr Brown for pointing out that in our article,¹ we incorrectly attributed the suggestion that the benefits of placebo have similarities with the benefits of psychotherapy to Dr Brown, when it should really be attributed to Dr Frank.²

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1. Tohen M, Jacobs TG, Grundy SL, McElroy SL, Banov MC, Janicak PG, Sanger T, Risser R, Zhang F, Toma V, Francis J, Tollefson GD, Breier A, for the Olanzapine HGGW Study Group. Efficacy of olanzapine in acute bipolar mania: a double-blind, placebo-controlled study. *Arch Gen Psychiatry*. 2000;47:841-849.
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**Eicosapentaenoic Acid
in Treatment-Resistant Depression**

Almost a third of patients with depression fail to respond to existing treatments, and new treatments are required. Epidemiological evidence about fish intake¹ and blood levels of the relevant fatty acids²⁻⁴ suggests that increased intakes of ω 3 fatty acids such as eicosapentaenoic acid (EPA) may be helpful. A mixture of EPA and docosahexaenoic acid has been reported to improve depression and the course of illness in bipolar disorder,⁵ but to date, there are no reports of treatment of unipolar depression using this approach.

Report of a Case. We report the case of a 21-year-old male student with a 7-year history of unremitting depressive symptoms. At age 19 years, pharmacotherapy was commenced owing to increasing illness severity, with prominent low self-esteem, insomnia, sadness, inner tension, poor appetite, poor concentration, increasing social phobia, lethargy, pessimistic thoughts, and suicidal thoughts. During the following year there was no response to a variety of antidepressants, hypnotics, and antipsychotic medication; his condition continued to deteriorate. A 2-month trial involving the addition of lithium carbonate to his antidepressant treatment was unsuccessful.

The patient was then referred to one of the authors (B.K.P.). At this time, he was actively suicidal, although he had been taking paroxetine hydrochloride (20-30 mg/d) for 10 months. His symptoms met the DSM-IV criteria for “major depressive disorder, recurrent.” His score on the Montgomery-Åsberg Depression Rating Scale (MADRS) was 32. Owing to very good parental support, it was decided not to admit the patient compulsorily to the hospital, despite the severity of his illness and the very high suicide risk. He agreed to take pure ethyl-EPA (ethyl ester of EPA; purity > 95%; esterified at the carboxyl end of the molecule; supplied as LAX-101; Laxdale Research, Stirling, Scotland) at a dose of 4 g/d.

Administration of ethyl-EPA led to a rapid improvement, including cessation of the previously unremitting severe suicidal ideation, within 1 month. Social phobia also improved dramatically. There was a progressive benefit, and after 9 months, his symptoms had disappeared altogether, giving the patient a MADRS

score of zero. Both he and his mother reported how different he had become. He no longer had any suicidal thoughts and was actively making plans for his future studies and career. The patient reported no adverse effects of the medication.

Comment. This case represents the first, and thus far, the only patient with unipolar major depression who has been treated by us with ω 3 fatty acids. As the only change in therapy during the 9-month period was the addition of EPA, and since the patient's depressive symptoms had previously continued to worsen, despite adequate trials with a range of standard medications, it seems likely that the clinical improvement was associated with the EPA.

The only known adverse effect of long-term treatment with gram quantities of pure ethyl-EPA is occasional initial loosening of the stools. It is not yet known how long EPA treatment should continue; to date, the patient has been treated for longer than 1 year and is currently in excellent health with no adverse side effects and a complete remission of his previous symptoms.

In view of the lack of effective drugs for treatment-resistant depression, double-blinded placebo-controlled trials of EPA are indicated.

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