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PUSHPAL DESARKAR, M.D., D.P.M.
ANUPAM THAKUR, M.D.
VINOD KUMAR SINHA, M.D., D.P.M.
*Ranchi, India*
*Jharkhan, India*

## Lipids, Hormones, and Gastric Bypass

To the Editor: I read with great interest the case presentation by Wei Jiang, M.D., and colleagues on psychosis after gastric bypass surgery (1). As a member of the house staff at their institution, I briefly assisted in the care of the patient and recall him as among the more acutely psychiatrically ill patients I have seen. Outside of the discussed concerns, additional questions were raised in regard to this case. I present the following two related points as worthy of further discussion.

First, brain tissue is composed largely of lipids (2). Although we know the effect of rapid weight loss on serum lipids and adipose tissue (3, 4), I am unaware of reports on the effects of bariatric surgeries and subsequent rapid weight loss on nervous tissue, especially in the central nervous system (CNS).

Second, adipose tissue is highly involved in many areas of steroid metabolism and other endocrine processes (5, 6), which also affect psychiatric illness and behavior. In addition, bariatric surgery is responsible for direct changes in hormones (7, 8), but there are few studies investigating its potential impact on the CNS.

Gastric bypass surgery is generally relatively well tolerated, and many of the changes result in improvements in general health, but we know little about the effect on psychiatric illness and behavior (9, 10). It is conceivable that the processes mentioned above may also have adversely affected the patient in the study by Dr. Jiang and colleagues, and these processes warrant further research.

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HEATH R. PENLAND, M.D.
*New Haven, Conn.*

## Dr. Jiang Replies

To the Editor: Thanks to Dr. Penland for bringing up these thought-provoking and challenging topics. I appreciate his contemplation and valiancy.

The role of lipids in brain function is significant. Thirty years ago, lipids were described in a great textbook of biochemistry as being unlike nucleic acids and proteins—that they "do not have information-carrying function" (1). With the series of convergent discoveries in the fields of neural development, synaptic physiology, and receptor pharmacology, the roles played by lipids and their receptors in brain function are being addressed in neuroscience.

Lipids comprise 50%–60% of the dry weight of the adult brain, of which approximately 35% are in the form of long-chain polyunsaturated fatty acids. These polyunsaturated fatty acids are derived through biosynthesis from their respective dietary essential fatty acid precursors, linoleic acid and $\alpha$-linolenic acid or directly from dietary sources such as eggs, fish, and meat or from single-cell oils.

Dietary fat profoundly affects gene expression through binding directly with transcription factors or through eicosanoid regulation of intracellular signaling cascades, which results in alterations in metabolism, growth, and cell differentiation (2). Chronic *N*-3 fatty acid deficiency has been found to reduce dopamine receptor binding and increase serotonin receptor density in the frontal cortex of both young and aged rats as well as to alter dopamine metabolism (3–5). A formula low in linoleic acid and $\alpha$-linolenic acid has been reported to result in low serotonin and dopamine levels in the frontal cortex of adult pigs (6).

The dynamic function of lipids, lipid signaling, was well described by Piomelli (7) as having four defining features: 1) the generation of informational diversity through permutation of simple structural units; 2) the "pervasive use of serial signaling"—that is, the application of a single biochemical pathway to multiple signaling needs; 3) the adoption of a signaling modality defined by the rapid on-demand response to primary signaling events, such as receptor activation; and 4) the localized nature of lipid-mediated signaling. Piomelli stated that in no other mammalian tissue do such features emerge more clearly than in the brain, where the roles of lipid messengers extend from the development of the neocortex to the processing of behavior. He further emphasized the diversity, the heterogeneity, and the complexity of the roles of lipids in the