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TO THE EDITOR: I would like to comment on the article by Judd Marmor, M.D., that appeared recently in Images in Psychiatry (1). Dr. Marmor wrote that Franz Alexander "was invited in 1930 by Robert Hutchins, then President of the University of Chicago, to become its Visiting Professor of Psychoanalysis—the first University Chair of Psychoanalysis in history."

Dr. Marmor's statement is true from a practical point of view since Alexander was the first *functioning* head or chair of psychoanalysis in history. However, the historical truth is that the first psychoanalyst who was appointed to be a professor of psychoanalysis was Sándor Ferenczi (2). He received this title at the University of Budapest in 1919 by the short-lived communist regime. After the change in regime, Ferenczi's appointment as the newly founded chair was not confirmed, so he lost the appointment before he was be able to begin to function as a university professor of psychoanalysis.

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Anorexia Nervosa and Gastrointestinal Tumors

TO THE EDITOR: As pointed out by Katherine A. Halmi, M.D., and Gladys Frankel, Ph.D., (1), the process of differential diagnosis between anorexia nervosa and anorexia due to gastrointestinal stromal tumors is sometimes problematic. The authors emphasized the importance of making a diagnosis based on positive criteria.

Nevertheless, even if the diagnosis of anorexia nervosa is evident in the case reported in their article, because the development of progressive malnutrition or cachexia is frequent in patients with gastrointestinal cancer, it still raises certain questions.

Cachexia syndrome is characterized by an involuntary weight loss of more than 5% of premorbid weight occurring within 6 months and often associated with anorexia and fatigue. Moreover, anorexia has been reported in patients with gastrointestinal stromal tumors, but unlike anorexia nervosa, it was not associated with voluntary weight loss and bingeing/purging behavior but was frequently associated with the presence of fever.

In this case, the negative criteria should also be considered, notably the absence of fever, fatigue, cachexia syndrome, and nausea and abdominal pain, which may have induced intentional anorectic behavior in the early onset of the disease.

Anorexia nervosa and cachexia are two distinct syndromes that may have synergistic effects in patients. Moreover, the occurrence of metastasis in the case report might have increased weight loss or, as pointed out by the authors, it might have been preceded by weight loss, which may lead to a perpetual cycle of maintaining weight loss and malnutrition. As the authors stated, when the tumor became a large mass, it could have created an early experience of satiety, and a highly restrictive diet might have been reinforced by undetected gastrointestinal stromal tumors.

Hence, this case report is an interesting and exceptional case of anorexia due to comorbid diagnoses. From a psychoneuroendocrinoimmunological point of view, this case deserves further attention.

Several studies in anorectic patients have found increased levels of pro-inflammatory cytokines, such as interleukin (IL) IL-1, IL-6, and tumor necrosis factor alpha (known for their anorexigenic effects), indicating autoimmune activation (2). Pathophysiological parallels have been drawn between the role of cytokines in cancerous cachexia and their putative involvement in the undernourished states observed in anorexia nervosa (3, 4). Tumor necrosis factor alpha, IL-1, IL-6, and interferon γ have been proposed as mediators of the cachectic process. It has been shown that the levels of these cytokines correlate with the progression of the tumors (5).

Therefore, it is not unreasonable to consider that the assay of pro-inflammatory cytokines, such as tumor necrosis factor alpha, in this case might have been a good marker of the course of the disease and might have helped to disentangle the evolution and the contribution of the two disorders to weight loss when we considered serum levels of this cytokine.

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Drs. Halmi and Frankel Reply

TO THE EDITOR: We agree with Dr. Guilbaud and his associates that measurement of pro-inflammatory cytokines may be helpful in following the progression of gastrointestinal stromal tumors. In fact, most patients with anorexia nervosa do not have elevated cytokine levels; thus, an increase in these

levels would provide further suspicion that metastases are occurring or increasing.

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Estradiol Effects on the Postmenopausal Brain

TO THE EDITOR: We commend Akira Kugaya, M.D., Ph.D., and colleagues (1) on their brief report on serotonin 2A (5-HT_{2A}) receptors in postmenopausal women. Characterization of the effects of gonadal steroids on neuroreceptor pharmacology and cognitive function holds great importance to clinical care and cognitive neuroscience research. Consistent with the article by Dr. Kugaya et al., we previously reported that 5-HT_{2A} receptor binding potential significantly increased in postmenopausal women during administration of transdermal estradiol, 0.1 mg/day for 8 to 14 weeks, followed by combined transdermal estradiol and progesterone, 100 mg b.i.d. (2 to 6 weeks), with positron emission tomography and the selective 5-HT_{2A} receptor radioligand [^{18}F]altanserin. Dr. Kugaya et al. correctly cited this publication as reporting a "subthreshold" effect of estradiol alone on increasing 5-HT_{2A} receptor binding potential in specific brain regions of interest. However, we alert readers to our more recent publication (2), in which our original image data were analyzed voxel by voxel using statistical parametric mapping, a technique similar to that applied by Dr. Kugaya et al. Consistent with the work of Dr. Kugaya et al., this approach showed that administration of estradiol alone increased 5-HT_{2A} receptor binding potential in multiple brain regions that had not been examined in our initial region-of-interest analysis (3), which included the right superior frontal gyrus, the right ventrolateral prefrontal cortex, the left inferior parietal cortex, and the left temporal polar cortex. Furthermore, in a post hoc analysis that employed a lower significance threshold for identifying voxels with increased 5-HT_{2A} receptor binding potential after estradiol treatment (the same threshold used by Dr. Kugaya et al.), we observed widespread increases in estradiol-related cortical 5-HT_{2A} receptor binding potential.

Given the clinical risks and benefits associated with the hormone replacement therapy regimens investigated in recent large-scale clinical trials (4, 5), mechanistic studies such as these may help shift the focus to alternate hormone replacement therapy regimens that may exert potentially beneficial effects on brain function. Both our study and that of Dr. Kugaya et al. lack the sensitivity needed to establish relationships between changes in 5-HT_{2A} receptor binding and cognitive function or emotional behavior, which minimizes the potential for making clinical inferences. The sensitivity of both studies was limited by small group sizes and ceiling/floor effects on neuropsychological test performance in cognitively intact euthymic women. The findings of these studies nevertheless support the initiation and inform the design of future studies aimed at investigating neurobiological bases for the potential neuropsychiatric benefits of such treatments in specific patient populations.

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Dr. Kugaya and Colleagues Reply

TO THE EDITOR: We agree with the points raised in the letter by Dr. Moses-Kolko et al. To clarify, we applied stringent statistical criteria (statistical parametric mapping voxel threshold of $p<0.01$) in our study and identified a large and significant increase (>5000 pixels with corrected $p=0.001$) in the right frontal area of the brain. Differences in sample size or methodology (including statistical parametric mapping statistics) may explain some discrepancies between the studies in affected brain areas.

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Terrorism and Psychiatric Disorders

TO THE EDITOR: Lynn E. DeLisi, M.D., et al. (1) reported a most interesting account of the reaction of New Yorkers to the events of Sept. 11, 2001, 3–6 months later. We wish to highlight one important finding they made, the higher risk faced by persons with psychiatric disorders when exposed to major terrorist events. The authors found that 63 individuals who were in previous psychiatric treatment, of the 1,009 adults that were interviewed, had significantly greater mean scores on the Davidson Trauma Scale. Earlier, also with regard to the events of September 11, Hoge and Pavlin (2) noted that based on behavioral health surveillance among military health system beneficiaries in the Washington, D.C., area, they found