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