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

KATHERINE A. HALMI, M.D.
GLADYS FRANKEL, PH.D.
White Plains, N.Y.

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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EYDIE L. MOSES-KOLKO, M.D.
CAROLYN CIDIS MELTZER, M.D.
PHIL GREER, M.S.
MERYL BUTTERS, PH.D.
SARAH L. BERGA, M.D.
GWENN SMITH, PH.D.
WAYNE C. DREVETS, M.D.
Pittsburgh, Pa.

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.

AKIRA KUGAYA, M.D., PH.D.
C. NEILL EPPERSON, M.D.
CHRISTOPHER H. VAN DYCK, M.D.
MASAHIRO FUJITA, M.D., PH.D.
ROBERT B. INNIS, M.D., PH.D.
New Haven, Conn.

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

no increase in visits to behavioral health clinics in the 22 weeks between Sept. 11, 2001, and Feb. 9, 2002, compared with a similar period 2 years earlier.

We explored selected health indicators on the effect of the El-Aqsa *intifada* on the residents of Jerusalem. Our city had been subjected to no less than five major terrorist events during the period October 2001 to December 2002 (the period we explored, although the *intifada* continues). One of the indicators we wish to report is the number of visits to governmental psychiatric outpatient clinics in the city. These well-staffed clinics provide free treatment and are located in different places in the city. Referrals are not required, and users could walk in according to their needs. We looked into the visits of users belonging to three age groups with regard to the following categories: 1) those who were new to the system, 2) those who returned to the clinic after at least a 5-year break, and 3) visits by patients under care.

We used time series analysis to study the data, taking into account inherent ongoing trends within the system. The results showed that there was a statistically significant increase in visits by patients who were under care, both adults and elderly, although there were no changes among the two other groups.

Our results appear to confirm both reports (1, 2). Breslau (3), among others, found that persons in psychiatric care are more vulnerable to major stressful events, such as those generated by terrorism. Ursano, quoted by Stephenson (4), alerted planners and administrators about the risk of taking away mental health personnel from the care of patients in order to address other possible terrorism-related mental health problems. In a forthcoming report, we will show the burden of care in other services of Jerusalem other than psychiatric.

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ITZHAK LEVAV, M.D.
ALEXANDER GRINSHPOON, M.D.
ILYA NOBIKOV, PH.D.
ALEXANDER PONIZOVSKY, M.D., PH.D.
Jerusalem, Israel

Pregnancy and Antidepressant Counseling

TO THE EDITOR: It was with great interest that we read the article by Adele C. Viguera, M.D., et al. (1) published recently. These results confirm what we have been aware of for many years: that pregnant women are not being counseled appropriately concerning drug therapy and reproductive risks.

The Motherisk Program is a counseling service for pregnant and lactating women and their health professionals, in which evidenced-based information is given on the safety/risk of drugs, chemicals, radiation, and infectious diseases to almost 40,000 callers/year. We published a study documenting the experiences of 36 women who had abruptly discontinued antidepressants or benzodiazepines upon finding out they were pregnant (2). All of the women reported discontinuation for fear of teratogenic risk, and 28 (77%) discontinued on the advice of their physicians. Despite receiving reassuring counseling that it would be appropriate to continue their medication, only 22 (61%) chose to do so (2).

To determine why these decisions were made, we are now carrying out a study to enroll women who are planning pregnancy or are in the first trimester who are taking an antidepressant. Two control groups of women have also been enrolled in the study: women taking nonpsychiatric drugs 1) on a long-term basis and 2) on a short-term basis. Our hypotheses are that there is still a stigma surrounding mental illness and that women are more cautious about taking a psychiatric drug during pregnancy. We asked the same questions of all three groups. Our preliminary results are that after all three groups had been advised that it was appropriate to continue their medication during pregnancy, 15% of the antidepressant group compared to 3.8% of the chronic medication group and 1.2% of the short-term treatment group decided to discontinue their drug. What we also found was that many factors come into play in the perception of teratogenic risk; however, in the determinants of decision making, the most important factor was the order in which the information was given to them, with the initial information having the most lasting effect (3).

We are sharing this information because we feel that it is an important area of research to ensure that women who are suffering from a mental illness are appropriately treated during pregnancy to ensure optimum conditions for both mother and child.

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ADRIENNE EINARSON, R.N.
LORI BONARI, B.SC.
GIDEON KOREN, M.D.
Toronto, Ont., Canada

Depression Treatment During Pregnancy

TO THE EDITOR: A clinical case conference by Victoria Hendrick, M.D., and Lori Altshuler, M.D. (1), addressed an urgent clinical dilemma: how to best treat depression during pregnancy. The authors correctly pointed out that clear guidelines for treating depression during pregnancy are lacking and that experts reach different conclusions about the best treatment in this situation. They provided a thorough review of treatment options, the results of published articles concerning morphological and behavioral teratogenesis, and the impact