suicidal behavior in contrast to major depression, where a diffuse abnormality in serotonergic function is found throughout the prefrontal cortex. Differences also exist in other brain regions between the findings in depression vs. suicidal behavior. Given that suicidal behavior is also associated with increased lifetime aggression and impulsivity, we have postulated that there is a fundamental deficiency in the restraint mechanisms located in the prefrontal cortex and the amygdala, in terms of aggression. We have evaluated serotonergic responses to fenfluramine using positron emission tomography (PET) with \(^{18}F\)-fluorodeoxyglucose (\(^{18}FDG\)) and found that there are abnormalities associated with depression and a specific abnormality in the prefrontal cortex associated with highly lethal suicidal behavior. The degree of this abnormality in depression is reduced by serotonin release with fenfluramine. The difference between individuals who have made low lethality suicide attempts and those who have made high lethality suicide attempts is also sensitive to the effects of serotonin release. These studies add to the body of literature implicating serotonergic function in suicidality, an abnormality that is independent of that associated with mood disorders.

### 20. BULIMIA NERVOSA: A DISTURBANCE OF SEROTONIN/ORBITAL FRONTAL CORTEX MODULATION?

**W.H. Kaye, G.K.W. Frank, C. Meltzer, J. Price, W.C. McConaha**

Western Psychiatric Institute and Clinic, Pittsburgh, PA 15213

Bulimia nervosa (BN), which tends to occur in adolescent women, is characterized by extremes of eating, mood, an impulse control. Recent studies suggest that BN is highly heritable and may involve a trait related disturbance of serotonin activity. For example, recovered BN women have increased levels of CSF 5-HIAA compared to control women (CW), but normal CSF HVA and MHPG concentrations. Positron emission tomography (PET) with serotonin radioligands, such as \(^{18}F\)altanserin, a 5-HT2A receptor antagonist, offers the potential for new understanding of previously inaccessible brain 5-HT function and its dynamic relation to receipt of serotonergic ligands. By using serially pre- and post-intervention, features that represent substantial advantages over postmortem assays.

**21. IMAGING THE SEROTONIN SYSTEM IN AGING AND LATE-LIFE NEUROPSYCHIATRIC DISORDERS**

**C.C. Meltzer**

Departments of Radiology and Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213

Serotonin (5-HT) plays a modulatory role in the central control of mood, cognitive function and a variety of human behaviors. Age effects on serotonergic function may be responsible for the normal spectrum of behavioral alterations observed in the elderly, and may contribute to the vulnerability of the elderly to depression. Further, pathologic changes in serotonergic function could be linked to mood and behavioral changes frequently accompanying Alzheimer’s disease (AD).

The recent development of selective markers for the 5-HT system, in conjunction with methodological advances in image processing, including partial volume correction, has made it now possible to quantitatively image important 5-HT markers in aging and late-life neuropsychiatric disorders. These include ligands for the 5-HT transporter, and the 5-HT1A and 5-HT2A receptors. The \(^{18}F\)-altanserin binding study of the 5-HT transporter, and the 5-HT1A and 5-HT2A receptors. The in vivo measurement of 5-HT markers provides a means to evaluate serotonergic function in early disease states and serially pre- and post-intervention, features that represent substantial advantages over postmortem assays.

PET imaging has verified a striking reduction in 5-HT1A receptor binding with age, and preliminary evidence suggests an interaction between gender and aging effects on the 5-HT1A receptor. These findings are in accord with the hypothesis that aging changes in serotonergic function may predispose the elderly to depression and behavioral alterations. Preliminary data on 5-HT PET imaging in depressed patients and in AD will also be reviewed. The long-term goals of this work are to further characterize the serotonergic profile of normal aging and to guide therapeutic approaches to late-life neuropsychiatric disorders.