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Impulsivity and prefrontal hypometabolism in borderline personality disorder

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Abstract

Prefrontal hypoperfusion and decreased glucose uptake in the prefrontal cortex (PFC) are found in violent criminal offenders, murderers and aggressive psychiatric patients. These abnormalities may be independent of diagnosis and associated with impulsive-aggression as a personality trait. Impulsive-aggression is a clinical characteristic of borderline personality disorder (BPD) where it is associated with assaultive and suicidal behaviors. We conducted FDG-PET studies in 13 non-depressed, impulsive female subjects with BPD and 9 healthy controls to look for abnormalities in glucose metabolism in areas of the PFC associated with regulation of impulsive behavior. Statistical Parametric Mapping-99 (SPM99) was used to analyze the PET data with Hamilton depression scores as covariate. Significant reductions in FDG uptake in BPD subjects relative to healthy controls were found bilaterally in medial orbital frontal cortex, including Brodmann's areas 9, 10 and 11. There were no significant areas of increased uptake in BPD subjects compared to control subjects. Covarying for measures of impulsivity or impulsive-aggression rendered insignificant the differences between groups. Decreased glucose uptake in medial orbital frontal cortex may be associated with diminished regulation of impulsive behavior in BPD.

Keywords: Positron emission tomography; Prefrontal cortex; Aggression; Suicide; Personality disorders; Fluorodeoxyglucose-F18

1. Introduction

Violent behavior is associated with disturbances in cerebral blood flow and glucose metabolism in imaging studies of aggressive psychiatric patients, violent criminal offenders and murderers (Soderstrom et al., 2000; Raine et al., 1997; Raine and Buchsbaum, 1996, for reviews). Compared to healthy controls, subjects ascertained by violent behavior show hypoperfusion or decreased glucose uptake in areas of prefrontal, frontal and temporal cortex. These aberrations may be independent of major mental disorders, substance use, or concurrent medication (Soderstrom et al., 2000). Among violent offenders, measures of frontal and temporal perfusion are inversely related to severity of psy-

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chopathy (Soderstrom et al., 2002), and are associated with impulsive-aggression rather than planned or 'predatory' aggression (Raine et al., 1998). Structural neuroimaging studies demonstrate reduction in the volume of prefrontal grey matter in aggressive subjects with antisocial personality disorders (ASPD) compared to controls, even after matching for co-morbid substance use or psychiatric disorders (Raine et al., 2000). By definition, such studies involve unusual populations, and are often conducted in highly specialized settings under unusual circumstances (e.g. pretrial examinations in forensic centers). They may be uncontrolled for co-morbid psychiatric diagnoses or effects of treatment. While important in their own right, the findings from such studies are difficult to generalize to psychiatric patients seen in community practice, who may demonstrate impulsivity and impulsive-aggression as symptoms of their disorders, though in less violent (or criminal) ways.

Impulsivity and impulsive-aggression are heritable traits of temperament that may contribute a biological diathesis to violent behavior (Barratt and Patton, 1983; Livesley et al., 1993, 1998; Coccaro et al., 1993). We have been studying these personality traits as risk factors for violent and suicidal behavior in the context of borderline personality disorder (BPD), a highly prevalent disorder (Swartz et al., 1990; Widiger and Weissman, 1991), defined, in part, by impulsivity in multiple areas of life and by recurrent suicidal behavior (DSM-IV). Among BPD subjects followed in our current longitudinal study, 58% have been involved 'occasionally or often' in physical fights as adults; 25% have used weapons against others. Impulsive-aggression in BPD may be self-directed, and predicts the number of lifetime suicide attempts, independent of co-morbid depression and substance abuse (Soloff et al., 2000a; Brodsky et al., 1997). With an average of three or more lifetime suicide attempts per patient (Soloff et al., 1994; Zisook et al., 1994) and a suicide completion rate of 3–9.5% (Stone, 1989), BPD is one of the most lethal psychiatric disorders, and provides a relevant clinical model for studying impulsivity and impulsive-aggression in the community setting.

A large body of experimental animal research, as well as clinical and laboratory observations in man, implicates the prefrontal cortex (PFC), especially the orbitofrontal cortex, as a site of 'executive function' in regulating the neural circuits that mediate impulsivity, response inhibition and impulsive-aggressive behavior (see Fuster, 1989, 1999; Weinberger, 1993; Damasio et al., 1994). Neuropsychological tests in impulsive subjects with BPD, antisocial behavior, conduct disorders, or other disorders of impulsivity show deficits in frontal lobe executive functions, especially cognitive processes involving goal-oriented planning, problem-solving set maintenance, selective attention and inhibitory control (Morgan and Lilienfeld, 2000; Stein et al., 1993; Burgess, 1992). We performed positron emission tomography (PET) with fluorodeoxyglucose-F18 (FDG) in impulsive, self-destructive subjects with BPD to look for disturbances of glucose metabolism in areas of the PFC associated with regulation of impulsive behavior.

2. Method

This study was approved by the Institutional Review Board of the University of Pittsburgh. Written informed consent was obtained from each participant. Physically healthy female subjects were recruited from ongoing longitudinal studies on BPD, from outpatient clinics of the Western Psychiatric Institute and Clinic, and by community advertisement. All subjects were examined for Axis I disorders, including psychoactive substance use disorders, by the Structured Clinical Interview for DSM-III-R (SCID; Spitzer et al., 1988) and Axis II disorders by the International Personality Disorders Examination (IPDE; Loranger et al., 1987). (All BPD subjects were participating in longitudinal studies that were instituted using DSM III-R.) BPD was diagnosed by the Diagnostic Interview for Borderline Patients (DIB, scaled score $\geqslant 7$), with a 2-year time frame (Gunderson et al., 1981), and by the IPDE, for lifetime diagnosis. Subjects were excluded for a *current* Axis I diagnosis of major depressive episode (MDE), though past episodes of MDE were allowed. Additional exclusionary criteria included: lifetime diag-