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Brief report

Lower cerebrospinal fluid homovanillic acid levels in depressed suicide attempters

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Abstract

Background: Studies suggest that the dopaminergic system is involved in the pathogenesis of major depression, Axis II disorders, and suicidal behavior. Depressed suicide attempters constitute a heterogenous group and important differences may exist between depressed suicide attempters with or without Axis II disorders. Therefore, we compared demographic and clinical parameters, and cerebrospinal fluid (CSF) homovanillic acid (HVA) levels in depressed suicide attempters *without comorbid Axis II disorders*, depressed non-attempters *without comorbid Axis II disorders*, and normal controls.

Methods: Thirty-one depressed subjects with a history of a suicide attempt, 27 depressed subjects without a history of a suicide attempt, and 50 healthy controls were included in the study. Subjects with comorbid Axis II disorders were excluded. Demographic and clinical parameters, and CSF HVA levels were examined.

Results: The two depressed groups did not differ with regard to depression, aggression, hopelessness, and total hostility scale scores. Depressed suicide attempters had higher current suicidal ideation scores compared to depressed non-attempters. Depressed suicide attempters had lower CSF HVA levels compared to depressed non-attempters ($t=4.4$, $df=56$, $p<0.0001$) and to controls ($t=-4.09$, $df=79$, $p<0.0001$). There was no difference in CSF HVA levels between depressed non-attempters and controls ($t<1$, $df=75$, NS).

Conclusions: Dopaminergic abnormalities are associated with suicidality but not with depression. The variability in the rates of comorbid Axis II disorders and in the prevalence of suicide attempters in different patient populations may affect both clinical and biological results of studies of mood disorders.

Keywords: Depression; Suicide; Cerebrospinal fluid; Homovanillic acid; Dopamine

1. Introduction

Low serotonergic activity is associated with suicidal behavior independently of psychiatric diagnosis (Mann, 2003; Sher and Mann, 2003). A possible role of altered dopaminergic function in suicidal behavior independently of depression has not been extensively studied.

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Cerebrospinal fluid (CSF) homovanillic acid (HVA), a metabolite of dopamine, reflects functional activity of the dopamine-containing neurons localized mainly in the substantia nigra pars compacta, the ventral tegmental area and the hypothalamus (Papeschi et al., 1971; Stanley et al., 1985; Blennow et al., 1993). The majority of dopamine cells, which synthesize approximately three-fourth of all of the dopamine in the brain, are located in the anterior midbrain or mesencephalon (Melchitzky et al., 2000). Whereas 5-hydroxyindolacetic acid (5-HIAA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) concentrations in lumbar CSF are thought to include some contributions from spinal cord and peripheral nervous system sources, lumbar CSF HVA exclusively reflects brain metabolism of dopamine (Post and Goodwin, 1978). It is important to note, however, that the results of CSF HVA studies may be affected by some non-specific factors such as the motor activity of the patient or the size of the sample (Asberg et al., 1984; Degrell and Nagy, 1990).

An association between CSF HVA levels and suicidality was found by Traskman et al. (1981), Montgomery and Montgomery (1982), Agren (1983), Roy et al. (1986), Roy et al. (1989), Jones et al. (1990), Engström et al. (1999) but not by Berrettini et al. (1986) and Cremniter et al. (1999). Post-mortem studies of suicides have also provided conflicting results reporting higher HVA concentrations in the hippocampus (Crow et al., 1984) and prefrontal cortex (Ohmori et al., 1992), lower dihydroxyphenylacetic acid (DOPA) in the basal ganglia (Bowden et al., 1997) and no change in cortex (Crow et al., 1984; Arranz et al., 1997).

The dopaminergic system also plays a role in the neurobiology of Axis II disorders. Dopamine abnormalities are reported in borderline personality disorder (Schulz et al., 1985; Szigethy and Schulz, 1997; Coccaro, 1998; Chotai et al., 1998; Chengappa et al., 1999; Rocca et al., 2002; Friedel, 2004), antisocial traits (Gabel et al., 1995; van Goozen et al., 1999; Vanyukov et al., 2000; Soderstrom et al., 2001; Gerra et al., 2003) and schizoid personality disorder (Blum et al., 1997; Rosmond et al., 2001), schizotypal (Siever et al., 1991, 1993; Siever and Davis, 2004; Abi-Dargham et al., 2004), and paranoid personality disorder (Rosmond et al., 2001).

Depressed suicide attempters frequently have comorbid Axis II disorders. Including both Axis II and non-Axis II subjects in prior studies could obscure the relationship between dopamine and suicidal behavior in patients with major depression. Indeed, depressed suicide attempters constitute a heterogeneous group and important differences may exist in attempt behavior between depressed suicide attempters with or without Axis II disorders. Therefore, to determine the relationship of dopaminergic function to major depression and to suicidal behavior, we compared CSF HVA levels in depressed suicide attempters *without comorbid Axis II disorders*, depressed non-attempters *without comorbid Axis II disorders*, and normal controls.

2. Methods

2.1. Subjects

Thirty-one depressed subjects with a history of a suicide attempt, 27 depressed subjects without a history of a suicide attempt, and 50 healthy controls participated in the study after giving written informed consent. The study was approved by the Institutional Review Board. All patients had a DSM-III-R diagnosis of major depressive disorder. Exclusion criteria included presence of any Axis II disorders; current substance use disorders; a cognitive disorder which interfered with the patient's ability to answer clinician-administered and self report rating scales; a history of head trauma resulting in coma; and more than mild mental retardation. The depressed subjects were divided into two groups according to the presence or absence of a history of a suicide attempt. A suicide attempt was defined as a self-destructive act committed with some intent to end one's life.

2.2. Diagnostic assessment

Patients were assigned DSM-III-R diagnoses following a structured clinical interview. Interrater reliability for the primary diagnosis was high ($\kappa = 0.90$). Current severity of depression was assessed by the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960) and Beck Depression Inventory (BDI) (Beck et al., 1961). Lifetime aggression was assessed with the Brown–Goodwin Aggression History Scale (Brown and Goodwin, 1986). Hostility was rated on the Buss–Durkee Hostility Inventory (Buss and Durkee et al., 1957), which includes subscales of assault, irritability, resentment, indirect hostility, negativism, suspiciousness, verbal hostility, and guilt. Current hopelessness was measured with the Beck Hopelessness Scale (Beck et al., 1974a). A lifetime history of all suicide attempts was recorded. The degree of suicide intent at the time of the most lethal suicide attempt was rated with the Suicide Intent Scale (Beck et al., 1974b). The Scale for Suicide Ideation (Beck et al., 1979) was used to measure the severity of suicidal ideation during the week prior to index hospitalization. The Recent Life