

Comorbid Psychopathy Is Not Associated with Increased D₂ Dopamine Receptor *TaqI* A or B Gene Marker Frequencies in Incarcerated Substance Abusers

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Introduction

Substance abuse and antisocial personality diagnoses such as psychopathy or antisocial personality disorder (ASP) each exhibit genetic underpinnings and share prominent comorbidity (Devor and Cloninger 1989; Crowe 1974; Schulsinger 1977; Smith and Newman 1990). Thus, shared underlying genetic factors may contribute to the pathogenesis of both disorders (e.g., Gorenstein and Newman 1980).

Linkage and association analyses can help to assess whether a specific gene for one disorder can independently or additively contribute to vulnerability to another (Baron et al, 1990). The genetic markers most strongly implicated in vulnerability to substance abuse are the A1 and B1 *TaqI* restriction fragment length polymorphisms (RFLPs) at the 3' and 5' ends of the dopamine D₂ receptor (DRD2) gene (Blum et al 1990; Cloninger 1991; Uhl et al 1992, 1993). Seven studies have compared *TaqI* A1 marker frequencies in substance abusers and controls assessed to exclude substance abuse (Amadeo et al 1992; Blum et al 1990, 1991; Comings et al 1991; Cook et al 1992; Parsian et al 1991; Smith et al 1992). Combined data from these seven studies reveals that 42.3% (254/600) of substance abusers and 19.4% (38/196) of assessed controls displayed the A1 marker (Table 1). Only two studies have examined the B1 marker in substance abusers and assessed controls (Blum et al 1993; Smith et al 1992). Of substance abusers 32.8% (104/317) and of controls 14.0% (12/86) displayed the B1 marker (Table 2). Other studies utilizing controls unassessed to exclude substance abuse have failed to find an association between the DRD2 gene and substance abuse (Bolos et al 1990; Gelemtier et al 1991; Turner et al 1992).

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Table 1. DRD2 *TaqI* A1 Frequencies in Caucasian Substance Abusers and Controls Assessed to Exclude Substance Abuse

Study	Substance abusers	Controls assessed to exclude substance abuse
Amadeo et al 1992	21/49 (42.9%)	2/20 (10.0%)
Blum et al 1990	14/22 (63.6%)	4/24 (16.7%)
Blum et al 1991	42/89 (47.2%)	6/31 (19.4%)
Comings et al 1991	63/156 (40.4%)	3/20 (15.0%)
Cook et al 1992	5/20 (25.0%)	6/20 (30.0%)
Parsian et al 1991	13/32 (40.6%)	3/25 (12.0%)
Smith et al 1992	96/232 (41.4%)	14/56 (25.0%)
Total	254/600 (42.3%)	38/196 (19.4%)
Current study		
Psychopathic substance abusers	10/30 (33.3%)	
Nonpsychopathic substance abusers	9/28 (32.1%)	
Total	19/58 (32.8%)	

The high comorbidity between antisocial personality disorders and substance abuse suggests that a DRD2 variant marked by these *TaqI* RFLPs may represent a common diathesis for these disorders. If so, DRD2 A1 or B1 markers should be present in greater proportions of antisocial substance abusers than in non-antisocial substance abusers because the subjects with *both* an antisocial personality disorder and substance abuse would be more likely to manifest a postulated genetic diathesis than individuals with substance abuse alone. Examination of DRD2 markers in small samples of alcoholics diagnosed with antisocial personality disorder by two different methods yielded indeterminate results (Bolos et al 1990; Parsian et al 1991).

Antisocial personality disorders and substance abuse are present at high frequencies in criminal offenders (Smith and Newman 1990). In the current study we examine DRD2 genotypes

Table 2. DRD2 *TaqI* B1 Frequencies in Caucasian Substance Abusers and Controls Assessed to Exclude Substance Abuse

Study	Substance abusers	Controls assessed to exclude substance abuse
Blum et al 1993	29/85 (34.1%)	4/30 (13.3%)
Smith et al 1992	75/232 (32.3%)	8/56 (14.3%)
Total	104/317 (32.8%)	12/86 (14.0%)
Current study		
Psychopathic substance abusers	8/30 (26.7%)	—
Nonpsychopathic substance abusers	8/28 (28.6%)	—
Total	16/58 (27.6%)	—

in prison inmates to test the hypothesis that the DRD2 A1 or B1 markers might appear more frequently in substance abusers with antisocial personality disorder than in nonantisocial substance abusers. Because DRD2 gene marker frequencies have not been assessed in prison inmates, we also compare our results with those previously described for nonincarcerated subjects. Diagnostic approaches assessing psychopathy (Cleckley 1976; Hare et al 1991) and ASP survey very similar antisocial behaviors. However, the DSM-III-R ASP diagnosis (American Psychiatric Association 1987) may reflect more environmental influences because it "is defined almost entirely by antisocial and criminal behaviors . . . and it fails to capture an important part of the clinical essence of psychopathy" (Hare 1990, p 68) reflected in personality traits. We have therefore focused on incarcerated individuals diagnosed with psychopathy who also meet criteria for substance abuse or dependence. Incarcerated substance-abusing nonpsychopaths were selected as a comparison group because of similarities in socioeconomic status (SES), background, and ethnicity.

Method

Subjects

A list was compiled of 80 Caucasian men who were inmates at a minimum security prison in southern Wisconsin, previously diagnosed as psychopaths or nonpsychopaths (Arnett et al 1993; Smith and Newman 1990) who were still incarcerated at the prison. These inmates were contacted about participation in the current study; seven inmates refused participation, five failed to meet criteria for DSM-III alcohol or drug abuse (American Psychiatric Association 1980), and eight were unavailable for participation or were misidentified as eligible for the study. Genotyping for two inmates recruited for the study was unsuccessful. The resulting sample of 58 inmates who volunteered for paid participation in this study under informed consent and confidentiality assurances included individuals who were: (1) 18 to 40 years of age; (2) diagnosed with lifetime DSM-III alcohol or drug abuse or dependence; (3) not psychotic; (4) free from psychotropic medication during recruitment and testing; and (5)

functioning at or above the fourth-grade level on achievement tests. Of nonpsychopaths 93% and of psychopaths 97% met DSM-III criteria for lifetime diagnoses of alcohol abuse or dependence. Of nonpsychopaths 57% and of psychopaths 63% met criteria for at least one DSM-III lifetime diagnosis of drug abuse or dependence. The most common drug diagnosis was cannabis abuse/dependence (32% of nonpsychopaths and 37% of psychopaths) followed by cocaine abuse (21% of nonpsychopaths and 27% of psychopaths). Many inmates had multiple alcohol and drug disorder diagnoses.

Clinical Assessment

A 75–100 min interview characterizing education, family life, relationships, parenthood, sexual history, work history, criminal history, medical history, and alcohol and drug use was supplemented by review of social services files to yield ratings on the Revised Psychopathy Checklist that assesses psychopathy with demonstrated reliability and validity in criminal offenders (Hare 1990; Hare et al 1991; Smith and Newman 1990). Twenty-eight subjects scoring 22 and below were designated as "controls" and 30 individuals scoring from 30 to 40 were designated "psychopaths"; subjects scoring from 23 to 29 were not recruited for the study. In this sample, 29 of 30 psychopaths met criteria for the DSM-III-R ASP diagnoses (American Psychiatric Association 1987); 1 of 28 controls received the ASP diagnosis.

The alcohol and drug use sections of the Diagnostic Interview Schedule, Version IIIA (DIS) were scored by computer to provide lifetime DSM-III (American Psychiatric Association 1980) alcohol and drug disorder diagnoses (Robins et al 1981; Smith and Newman 1990). The Shipley Institute of Living Scale (Zachary 1986) provided age-corrected estimates of WAIS-R full-scale IQ.

RFLP Analysis

Deoxyribonucleic acid (DNA) was extracted from samples of 10 cc venous blood, digested with *TaqI* enzyme, separated by agarose gel electrophoresis, immobilized on nylon membranes, and hybridized with pHD2-9 detecting A1, A2, and A3 markers, and λ HD2G2 detecting B1 and B2 markers as previously described (Miller et al 1988; Smith et al 1992). Washing, autoradiography, and interpretation of Southern band patterns were performed as described (Smith et al 1992). After *TaqI* A RFLP status was determined, 32 P decay or blot stripping with 2 mmol/L tris(hydroxymethyl)methylamine (pH 8), 1 mmol/L ethylenediamine tetraacetic acid (EDTA), and 0.1% sodium dodecylsulfate (SDS) at 65°C for 30 min allowed rehybridization of the same blots with hybridization probe for *TaqI* B ascertainment.

Statistical Analyses

Analysis of variance (ANOVA) was used to test for age, education, and IQ differences between psychopaths and controls. Chi-square analysis was used to test association of DRD2 A1 and B1 markers with psychopathy.

Results

Of controls 32.1% (9/28) and of psychopaths 33.3% (10/30) displayed at least one copy of the *TaqI* A1 marker (A1/A1 or A1/A2); no significant association for the *TaqI* A1 marker and psychopathy was detected ($\chi^2 = 0.009$, NS). Similarly, no group difference was found for the *TaqI* B1 marker: 28.6% (8/28) of controls and 26.7% (8/30) of psychopaths displayed the B1 marker ($\chi^2 = 0.26$, NS). The two groups were similar in age (28.2 versus 28.4 years, for psychopaths and controls, respectively; $F(1,55) = 0.11$, NS), education [12.0 versus 11.3 years; $F(1,55) = 2.91$, NS], and IQ [98.3 versus 96.7; $F(1,55) = 0.19$].

When psychopathic and nonpsychopathic substance-abusing offender groups were combined, 32.8% of the subjects displayed the *TaqI* A1 RFLP and 27.6% displayed the B1 marker. Comparison of these frequencies with frequencies reported in previous studies for control subjects assessed to exclude substance abuse (see Tables 1 and 2) revealed significant associations for the A1 marker ($\chi^2 = 4.60$, $p < 0.05$) and the B1 marker ($\chi^2 = 4.11$, $p < 0.05$). Similar analyses comparing substance-abusing offenders in the current study with substance abusers in other studies (see Tables 1 and 2) revealed no statistically significant differences in DRD2 marker frequencies for either marker ($\chi^2 = 2.00$, NS, for A1; $\chi^2 = 0.61$, NS, for B1).

Discussion

This study tested the hypothesis that inmates with both psychopathy and substance abuse would display DRD2 A1 and B1

markers more frequently than nonpsychopathic substance-abusing inmates. Results revealed no gene marker frequency differences between the groups. These findings are in accord with results reported in two other studies that examined a total of 18 alcoholics with ASP (Bolos et al 1990; Parisian et al 1991): A1 marker frequencies in ASP-disordered alcoholics did not differ from comparison groups of alcoholics without ASP.

The incarcerated substance abusers in the present study displayed A1 and B1 marker frequencies similar to those reported elsewhere for nonincarcerated substance abusers (Uhl et al 1992). These data provide no evidence that substance-abusing prison inmates are more likely to display the A1 or B1 markers than nonincarcerated substance-abusing individuals, although our incarcerated substance abusers did display A1 and B1 marker frequencies higher than those found in nonincarcerated populations free of substance abuse (Uhl et al 1992). Nevertheless, the results of the current study should be considered preliminary given the relatively small sample size of offenders.

Psychopathy, substance abuse, and DRD2 alleles marked by the *TaqI* A1/B1 haplotype could be interrelated in several possible ways. Because we identified no psychopaths free from substance abuse, the present results cannot completely exclude modest DRD2 influences on psychopathy that might be masked by the substance-abuse comorbidity. Taken together with other results, however, the current data fit best with the lack of a substantial DRD2 gene association with psychopathy in substance abusers.

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