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Monoamine Oxidase-A Genetic Variants and Childhood Abuse Predict Impulsiveness in Borderline Personality Disorder

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Objective: Impulsivity is a core feature of borderline personality disorder (BPD) and antisocial personality disorder (ASPD) that likely arises from combined genetic and environmental influences. The interaction of the low activity variant of the monoamine oxidase-A (MAOA-L) gene and early childhood adversity has been shown to predict aggression in clinical and non-clinical populations. Although impulsivity is a risk factor for aggression in BPD and ASPD, little research has investigated potential gene-environment (G×E) influences impacting its expression in these conditions. Moreover, G×E interactions may differ by diagnosis.

Methods: Full factorial analysis of variance was employed to investigate the influence of monoamine oxidase-A (MAO-A) genotype, childhood abuse, and diagnosis on Barratt Impulsiveness Scale-11 (BIS-11) scores in 61 individuals: 20 subjects with BPD, 18 subjects with ASPD, and 23 healthy controls.

Results: A group×genotype×abuse interaction was present ($F(2,49)=4.4$, $p=0.018$), such that the interaction of MAOA-L and childhood abuse predicted greater BIS-11 motor impulsiveness in BPD. Additionally, BPD subjects reported higher BIS-11 attentional impulsiveness versus ASPD participants ($t(1,36)=2.3$, $p=0.025$).

Conclusion: These preliminary results suggest that MAOA-L may modulate the impact of childhood abuse on impulsivity in BPD. Results additionally indicate that impulsiveness may be expressed differently in BPD and ASPD.

KEY WORDS: Antisocial personality disorder; Borderline personality disorder; Early adverse experiences; Impulsivity; Monoamine oxidase A.

INTRODUCTION

Highly impulsive behavior is central to the phenomenology of both borderline personality disorder (BPD) and antisocial personality disorder (ASPD). Impulsivity is a multi-dimensional neuropsychological construct that in the broadest terms denotes the propensity to engage in maladaptive or problematic behaviors.[1] Several subtypes of impulsivity have been described that likely reflect distinct neural processes under genetic control.[2,3] Clinically, trait impulsivity has been linked to different forms of aggressive behavior in BPD and ASPD.[4-7]

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BPD patients score higher on the Barratt Impulsiveness Scale-11 (BIS-11),[8] a self-report measure tapping cognitive, behavioral, and nonplanning aspects of impulsivity, than healthy controls[9-11] and other clinically impulsive groups.[9,12] Individuals with ASPD similarly endorse higher BIS-11 scores relative to their healthy peers.[13,14] Number of ASPD symptoms has additionally been shown to predict BIS-11 motor impulsivity scores in a university sample.[15] To the best of our knowledge, only one study has directly compared indices of impulsive behavior in BPD and ASPD.[16] All of the subjects in this previous investigation had alcohol dependence and those with comorbid BPD obtained greater total BIS-11 scores than subjects with ASPD.

Evidence suggests that adverse childhood experiences may relate to the impulsivity of BPD and ASPD. In a large, non-clinical sample of young adults, childhood abuse was shown to exert direct effects on both trait disinhibition and borderline features.[17] In a cohort of male perpetrators of intimate partner violence, childhood mal-

treatment was associated with manifestation of BPD and ASPD symptoms, which, in turn, predicted greater BIS-11 scores.[18] A relationship between impulsive psychopathic traits and childhood sexual abuse has also been reported in a sample of sex offenders, many of whom would meet diagnostic criteria for ASPD.[19]

Heritable influences may also underlie expression of impulsive BPD/ASPD phenotypes. One genetic marker of interest is monoamine oxidase-A (MAO-A), an X-linked gene whose protein product degrades monoamine neurotransmitters such as serotonin, norepinephrine, and dopamine linked to manifestation of impulsive behavior.[20,21] A variable nucleotide tandem repeat (VNTR) polymorphism in the human MAO-A promoter region has been shown to influence transcriptional efficiency in an allele-specific manner depending on the number of copies of the VNTR. High activity MAO-A alleles (MAOA-H), which comprise 3.5 or 4 VNTR copies, are transcribed 2-10 times more efficiently than low activity alleles (MAOA-L), which contain 2, 3, or 5 copies.[22] MAO-A allelic variants are associated with BPD[23] and ASPD.[24] Impulsive aggression also shows a relation with the low transcription MAO-A allele in healthy samples.[25] Therefore, investigating whether MAO-A gene function is related to the impulsivity of ASPD and BPD is a potentially important line of inquiry. Examining how environmental effects moderate genetic risk for impulsivity can provide a more fulsome understanding of how adverse childhood experiences affect the development of impulsive behaviors. A growing body of literature indicates that male and female carriers of MAOA-L who experienced childhood maltreatment exhibit elevated rates of aggression and antisocial behavior, some of which may have been driven by impulsive action.[26,27] By contrast, much less is known about whether this gene-environment (G×E) combination predisposes to trait impulsiveness. Because trait impulsivity is a powerful risk factor for conduct-disordered behavior and aggression,[28] addressing this gap in the literature could refine our knowledge of G×E influences predisposing to violence. One of the first studies to tackle this question found that BIS-11 scores were higher among males with MAOA-H who had reported early childhood abuse. However, a cluster B personality disorder diagnosis was exclusionary in this investigation.[29] As far as we are aware, no study has examined these G×E relationships in personality disorder samples. We decided to study BPD and ASPD as separate groups for several reasons. First, there is now clear consensus in the literature that BPD and ASPD are distinct conditions.[30] Second, positron emission tomography studies have shown that MAO-A total distribution volume, a measure of MAO-A brain density, is different in BPD versus ASPD.[31,32] Third, impulsive behavior in BPD is often associated with self-harming or suicidal behavior and externalized aggression,[33] whereas the impulsivity of ASPD mainly involves harm toward others.[7,34]

To explore potential G×E relationships in personality disorders, we examined the association of diagnosis, MAO-A genotype, and history of childhood abuse with subtypes of trait impulsiveness. Because the aggression of BPD and ASPD is closely tied to high impulsivity and robust linkages have been described between the MAOA-L allele, childhood abuse, and aggression, we hypothesized that the MAOA-L genetic variant and history of childhood abuse would interact to predict greater trait impulsiveness in BPD and ASPD. We did not make specific predications as to whether certain impulsivity subtypes would differ in the personality disorder groups given the lack of research in this area. As such, we considered our investigation an exploratory analysis.

METHODS

Participants

All study components were approved by the Research Ethics Board for Human Subjects at the Centre for Addiction and Mental Health, Toronto, ON, Canada. Each participant provided written consent after study procedures had been explained. A subset of the ASPD and BPD subjects was enrolled in previous neuroimaging studies conducted by our group.[31,32] In total, 61 subjects participated in the current study: 18 subjects with ASPD, 20 subjects with BPD, and 23 healthy controls.

Personality Disorder Subjects

ASPD subjects

Subjects with ASPD were recruited from the community and federal correctional services halfway houses. ASPD was diagnosed following clinical assessment and use of the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II)[35] by a forensic psychiatrist (NJK), who also administered the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I).[36] To rule out confounds of major mood or psychotic disorders, exclusion criteria included a history of depression, mania, hypomania, or psychotic illness. Current substance abuse or dependence (except alcohol) and comorbid BPD were also exclusionary.

BPD subjects

BPD participants were recruited from the community, inpatient psychiatric wards, and the dialectical behavior therapy clinic at our institution. BPD subjects were clinically assessed by NJK using the SCID-I and SCID-II. Bipolar disorder, psychotic illness, comorbid ASPD, and current substance abuse or dependence were designated as exclusion criteria.

Control Subjects

Healthy controls were recruited from the community and were clinically assessed by NJK with the SCID-I and SCID-II. Healthy controls had no history of psychiatric illness.

Additional Study Criteria

All study participants were medication free, non-smoking, and provided negative urine toxicology tests for illicit substances.

Measures

Impulsivity measures

Barratt Impulsiveness Scale-11 (BIS-11)

The BIS-11 is self-report instrument indexing an impulsivity construct that consists of three subscales: motor impulsiveness, attentional impulsiveness, and non-planning impulsiveness. BIS-11 total score shows good internal consistency in healthy and psychiatric samples.[8] Whereas the motor impulsiveness subscale indexes acting without thinking and a lack of perseverance, the attentional impulsiveness subscale reflects cognitive disturbance and the inability to remain focused on an immediate task, and the nonplanning impulsiveness subscale captures lack of self-control.[37] BIS-11 impulsivity data for a subset of the BPD and ASPD participants have been reported previously.[31,32]

Childhood Trauma Questionnaire Short Form (CTQ-SF)

The CTQ-SF is a self-report measure that retrospectively assesses several categories of childhood abuse and neglect.[38] The CTQ-SF demonstrates good construct validity for assessing childhood maltreatment across clinical and non-clinical samples. Cronbach alpha scores for the sexual and physical scales exceed 0.90, indicative of excellent internal consistency.[39] The 10 items indexing physical abuse and sexual abuse factor scores (five items each) were measured in the current study. Items follow a Likert-type response style from 1 to 5 and are organized to reflect the frequency of abusive experiences (never true, rarely true, sometimes true, often true, very often true). History of childhood abuse was designated by a positive endorsement of any of the physical abuse or sexual abuse items.

Psychopathy Checklist-Revised (PCL-R)

The PCL-R[40] is a clinician-rated instrument that assesses interpersonal and behavioral features of psychopathy. The PCL-R includes 20 items that are rated from 0 to 2 based on whether the trait is present (*0*=no; *1*=maybe; *2*=yes). Official criminal records in combination with a clinical assessment were used to score the PCL-R. PCL-R data were available for the ASPD and healthy participants.

Genetics

The MAO-A VNTR locus was amplified using standard PCR procedures with primers as previously described.[41] Minor changes were implemented, including labeling the forward primer with 5' HEX modifier, to allow for electrophoresis and visualization on a capillary sequencer. Briefly, 125 ng total genomic DNA was combined with 1× PCR_x amplification buffer, 1.5 mM $MgSO_4$, and 1×PCR_x enhancer solution that accompanied the Invitrogen^{TM} PCR_x Enhancer Kit (ThermoFisher Scientific, Waltham, MA, USA), along with 0.2 mM of each dNTP, 0.0975 μg of each primer, and 0.5 U Taq polymerase in a total reaction volume of 20 μL. Cycling conditions were as previously described[41] with an additional denaturation step of 5 minutes at 95°C. One microlitre of the amplified product was electrophoresed and visualized using the ABI 3130 Genetic Analyzer system and GeneMapper software (ThermoFisher Scientific). Because the MAO-A gene is located on the X chromosome, males are hemizygous and females are heterozygous or homozygous at this locus. Individuals with 2, 3, or 5 copies of the MAO-A VNTR were classified as MAOA-L carriers, while those with 3.5 or 4 copies were classified as MAOA-H carriers. Female heterozygotes were categorized as MAOA-L carriers, consistent with previous research.[42]

Statistical Analysis

Full factorial analysis of variance (ANOVA) was specified to investigate G×E interactions contributing to impulsivity subtypes. Predictor variables included diagnostic group, MAO-A genotype, and childhood abuse. Dependent variables included BIS-11 motor, nonplanning, and attentional subscale scores. Separate models were cre-

ated for each dependent variable given the high degree of correlation among outcome variables. *Post-hoc* tests were conducted using independent samples *t* tests. Group comparisons of demographic, clinical, and impulsivity data were achieved using chi square tests, independent samples *t* tests, and Mann-Whitney *U* tests. Pearson correlations tested the relationship between impulsivity measures. The *p* values less than 0.05 were considered significant for each test. For the statistic analyses, IBM SPSS Statistics for Windows, version 24.0 (IBM Co., Armonk, NY, USA) was used.

RESULTS

Clinical and Demographic Data

As presented in Table 1, groups were similar in age, ancestry, and frequency of the low expression MAO-A allele. An independent samples *t* test similarly revealed no difference in age between the BPD and ASPD groups: $t(1,36)=1.075$, $p=0.29$. VNTR allele frequencies for the healthy group were similar to results obtained from other samples.[22] Groups showed differences in education level. *Post-hoc* tests revealed that ASPD participants completed fewer years of education compared with the healthy group ($p=0.005$). Personality disorder groups did not differ in years of education completed ($p=1.0$). Groups differed in frequency of self-reported childhood abuse. Abuse was more common in BPD and ASPD subjects compared with healthy controls (BPD vs. health: $\chi^2(1)=27.8$, $p<0.001$; ASPD vs. health: $\chi^2(1)=14.7$, $p<0.001$). BPD and ASPD groups did not differ in frequency of childhood abuse ($\chi^2(1)=0.16$, $p=0.18$).

Table 1. Demographic and clinical characteristics

Characteristic	BPD subjects (n=20)	ASPD subjects (n=18)	Healthy controls (n=23)
Age (yr)[a]	33.4±11.0	36.8±8.7	34.8±8.0
Ancestry (%)[b]			
Caucasian	65.0	50.0	54.2
African Canadian	10.0	25.0	4.2
Asian	15.0	15.0	29.2
Other	10.0	10.0	12.5
Education (yr)[a]*	13.9±2.3	13.8±2.4	16.0±1.8
Childhood abuse (%)[b]**	85.0	70.0	16.7
Low MAO-A (%)[b]	30.0	55.6	43.5
PCL-R[c]***		25.8±6.1	2.9±2.5

Values are presented as mean±standard deviation or percent only. BPD, borderline personality disorder; ASPD, antisocial personality disorder; MAO-A, monoamine oxidase-A; PCL-R, Psychopathy Checklist-Revised.
[a]One-way analysis of variance; [b]chi-square; [c]Mann-Whitney *U* test; *$p=0.001$, **$p<0.001$, ***$p<0.0001$.

Correlations between Impulsivity Measures

Scores for each BIS-11 subscale were highly and significantly correlated with each other in the total sample ($r=0.67$ to 0.71; all p values <0.001).

Models Testing G×E Interactions on Impulsivity Measures

BIS-11 motor impulsiveness

A three-way ANOVA yielded an effect of group on BIS-11 motor impulsiveness (Table 2). Motor impulsiveness scores were higher in the BPD (mean=29.7, standard deviation [SD]=6.7) and ASPD (mean=30.2, SD=5.1) groups compared with the healthy group (mean=21.0, SD=6.7; BPD vs. health: $t(1,41)=3.7$, $p<0.001$; ASPD vs. health: $t(1,39)=4.3$, $p<0.001$). No difference in motor impulsiveness scores emerged between ASPD and BPD groups ($t(1,36)=0.25$, $p=0.80$). A group×genotype×abuse

Table 2. Dependent variable: Barratt motor impulsiveness

Source	Type III sum of squares	df	Mean square	F	Sig.
Corrected model	1,116.660*	11	101.515	4.920	0.000
Intercept	23,534.901	1	23,534.901	1,140.615	0.000
Groups	460.851	2	230.425	11.168	0.000
Abuse	0.002	1	0.002	0.000	0.992
MAO-A	16.581	1	16.581	0.804	0.374
Groups×abuse	6.482	2	3.241	0.157	0.855
Groups×MAO-A	106.194	2	53.097	2.573	0.087
Abuse×MAO-A	15.870	1	15.870	0.769	0.385
Groups×abuse×MAO-A	180.225	2	90.113	4.367	0.018
Error	1,011.042	49	20.634		
Total	44,283.980	61			
Corrected total	2,127.702	60			

MAO-A, monoamine oxidase-A; df, degrees of freedom; Sig., significance.
*R squared=0.525 (adjusted R squared=0.418).

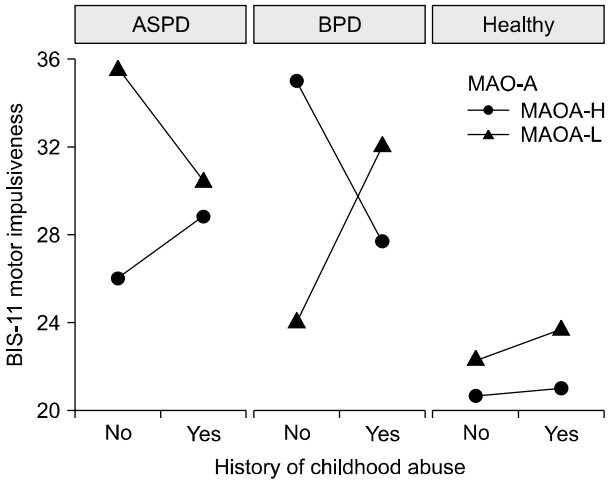

Fig. 1. Three-way interaction indicating that in the bordeline personality disorder (BPD), the combination of the MAOA-L genotype and history of childhood abuse was associated with greater BIS-11 motor impulsiveness scores.
ASPD, antisocial personality disorder; MAO-A, monoamine oxidase-A; MAOA-H, high activity MAO-A alleles; MAOA-L, low activity MAO-A alleles; BIS-II, Barratt Impulsiveness Scall-II.

interaction emerged from the model ($F(2,49)=4.4$, $p=0.018$) (Fig. 1). Among BPD subjects, the interaction of MAOA-L genotype and history of childhood abuse predicted BIS-11 motor impulsiveness scores. In the ASPD subsample, motor impulsiveness did not differ according to abuse history for either genotype (MAOA-L/abuse: mean=30.4, SD=4.0 vs. MAOA-L/no abuse: mean=35.5, SD=3.5; $t(1,8)=1.4$, $p=0.16$; MAOA-H/ abuse: mean=28.8, SD=4.0 vs. MAOA-H/no abuse: mean=26.0, SD=1.7; $t(1,8)=-0.8$, $p=0.40$). Similarly, in the healthy sample, motor impulsiveness scores did not depend on childhood abuse for either genotype (MAOA-L/abuse: mean=23.7, SD=0.6 vs. MAOA-L/no abuse: mean=22.3, SD=6.3; $t(1,8)=-0.4$, $p=0.66$; MAOA-H/abuse: mean=21.0, SD=20.8 vs. MAOA-H/no abuse: mean=20.7, SD=3.4; $t(1,11)=-0.07$, $p=0.94$).

BIS-11 attentional impulsiveness

An effect of group was observed for BIS-11 attentional impulsiveness scores (Table 3). BPD (mean=23.4,

Table 3. Dependent variable: Barratt attentional impulsiveness

Source	Type III sum of squares	df	Mean square	F	Sig.
Corrected model	968.449*	11	88.041	4.830	0.000
Intercept	11,572.015	1	11,572.015	634.838	0.000
Groups	329.105	2	164.552	9.027	0.000
Abuse	0.653	1	0.653	0.36	0.851
MAO-A	92.972	1	92.972	5.100	0.028
Groups×abuse	6.716	2	3.358	0.184	0.832
Groups×MAO-A	51.295	2	25.648	1.407	0.255
Abuse×MAO-A	10.669	1	10.669	0.585	0.448
Groups×abuse×MAO-A	47.970	2	23.985	1.316	0.278
Error	893.186	49	18.228		
Total	22,489.883	61			
Corrected total	1,861.636	60			

MAO-A, monoamine oxidase-A; df, degrees of freedom; Sig., significance.
*R squared=0.520 (adjusted R squared=0.413).

Table 4. Dependent variable: Barratt nonplanning impulsiveness

Source	Type III sum of squares	df	Mean square	F	Sig.
Corrected model	1,750.635*	11	159.149	5.063	0.000
Intercept	24,847.522	1	24,847.522	790.407	0.000
Groups	732.905	2	366.453	11.657	0.000
Abuse	0.349	1	0.349	0.011	0.916
MAO-A	15.551	1	15.551	0.495	0.485
Groups×abuse	33.497	2	16.748	0.533	0.590
Groups×MAO-A	63.207	2	31.604	1.005	0.373
Abuse×MAO-A	0.418	1	0.418	0.013	0.909
Groups×abuse×MAO-A	72.419	2	36.209	1.152	0.324
Error	1,540.382	49	31.436		
Total	48,356.000	61			
Corrected total	3,291.016	60			

MAO-A, monoamine oxidase-A; df, degrees of freedom; Sig., significance.
*R squared=0.532 (adjusted R squared=0.427).

SD=6.3) and ASPD (mean=19.0, SD=4.7) groups reported greater attentional impulsiveness than healthy controls (mean=15.0, SD=6.4; BPD vs. health: $t(1,41)=4.3$, $p<0.001$; ASPD vs. health: $t(1,39)=2.2$, $p=0.035$). Among the personality disorder groups, BPD participants reported greater attentional impulsiveness than ASPD subjects: $t(1,36)=2.3$, $p=0.025$. The three-way interaction effect was not significant.

BIS-11 nonplanning impulsiveness

There was an effect of group for BIS-11 nonplanning impulsiveness scores (Table 4). BPD (mean=32.7, SD=8.5) and ASPD (mean=30.1, SD=6.4) subjects had higher scores than healthy participants (mean=21.2, SD=8.6; BPD vs. health: $t(1,41)=4.4$, $p<0.001$; ASPD vs. health: $t(1,39)=3.7$, $p<0.001$). No difference in scores emerged between ASPD and BPD groups ($t(1,36)=1.1$, $p=0.30$), and the three-way interaction effect was not present.

When all analyses were re-run and education level was included as a covariate, results remained unchanged.

DISCUSSION

As far as we are aware, this investigation is the first to highlight G×E interactions relevant to the expression of impulsivity subtypes in personality disorders characterized by high impulsiveness. Consistent with our main hypothesis, we found that the low expression MAO-A genetic variant in combination with a history of childhood abuse predicted greater motor impulsiveness among the BPD participants. An additional study finding is that BPD subjects reported greater attentional impulsiveness compared with ASPD participants. Overall, our results suggest that MAO-A gene effects may moderate the influence of early adverse experiences on risk for increased impulsivity among individuals with BPD. Differences between ASPD and BPD groups further highlight the notion that these disorders have distinct biological markers. We also propose that the G×E effects on impulsivity detected in the BPD subsample have relevance for understanding previous work linking the MAOA-L allele and childhood abuse to aggression and/or conduct-disordered behavior.

Our principal finding is that a history of childhood maltreatment predisposed to greater motor impulsiveness among MAOA-L but not MAOA-H carriers with BPD. Previous investigations that explored links between childhood abuse and trait impulsivity have not always detected associations,[43] possibly because potential G×E interactions were not examined. Emotional dysregulation is a cardinal feature of BPD closely tied to trait motor impulsiveness.[44] Moreover, greater BIS-11 motor impulsiveness scores in BPD are associated with functional brain changes in regions linked to emotional control.[45] Interestingly, individuals who score high on the BIS-11 motor impulsiveness subscale require more effort to inhibit emotionally arousing stimuli, as evidenced by greater deflection of frontal event-related potential components.[46] MAO-A genetic variation may also influence emotional processing linked to inhibitory control. For example, MAOA-L carriers in one functional magnetic resonance imaging study exhibited dampened activation of prefrontal regulatory brain regions when presented with fearful and angry faces.[47] The MAO-A gene promoter region is subject to epigenetic modification,[48] and childhood abuse is also associated with genome-wide methylation patterns of gene promoter regions in adult DNA.[49] Therefore, one interpretation of our findings is that early adverse experiences modulate expression of the low-activity MAO-A allele to influence brain function underpinning motor impulsiveness.

Examining the interplay between risk genes, adverse environmental influences, and manifestation of lower-order personality traits, such as impulsivity, can shed light on G×E mechanisms predisposing to more complex behavioral phenomena in BPD. Although violence in BPD is often conceptualized as self-harming or suicidal behavior, violence directed toward others is a common feature of the disorder.[50] Impulsivity increases risk for externalized aggression among individuals with high BPD features.[51] Identifying G×E interactions in BPD that predict unidimensional traits linked to aggression could, therefore, provide additional interpretation to G×E interactions studies that tested broad-based forms of violent behavior as outcome measures.

The lack of an association between MAO-A, childhood adversity, and impulsivity in the ASPD subsample could relate to the high level of comorbid psychopathic traits. The mean PCL-R score for the ASPD group was 25.8, indicative of high psychopathic features. Since psychopathic symptoms, including impulsive antisociality, show high heritability,[52] G×E influences may be less relevant to development of impulsive symptoms in ASPD subjects with high psychopathy.

Another main study finding to emerge was that BPD participants reported greater attentional or cognitive impulsiveness compared with ASPD subjects. Attentional impulsiveness is elevated in adults with attention deficit

hyperactivity disorder (ADHD),[53] a neurodevelopmental condition that may exist as a continuum of quantitative traits.[54] Although ADHD is frequently comorbid with BPD and ASPD,[55,56] it shows stronger links with BPD.[57] We did not assess our study participants for ADHD. Yet, attentional impulsiveness is correlated with other measures of ADHD symptom severity.[58] Because attentional problems relate to poor functional outcomes in BPD[59] and greater ADHD symptom burden predicts more borderline symptoms,[60,61] we suggest that attentional impulsiveness may be of greater relevance to the psychopathology of BPD compared with ASPD. This supposition is bolstered by data presented in one study indicating that the effect size for differences in BIS-11 subscale scores between ASPD and healthy controls was smallest for attentional impulsiveness.[13]

We acknowledge several limitations of our investigation. First, the smaller group sizes may have limited the ability to detect additional G×E interactions present in a larger cohort. Although one option would have been to combine ASPD and BPD participants into a single group to increase study power, we were interested in exploring differences between the two disorders for the important reasons noted above. We would also add that the stringent exclusion criteria applied to the clinical groups (e.g., no smoking or substance use) increased the difficulty of recruiting participants. However, these restrictions enabled us to study personality disorder phenotypes that were free of major confounds. Second, we focused our analyses on self-report aspects of impulsivity and did not include behavioral measures. We opted for the former method, because examining genetic contributions to impulsiveness was a primary study objective, and trait-based impulsivity measures tend to show high heritability.[62-64] Third, the majority of our BPD subjects were female while the ASPD and healthy control groups were all male. Therefore, we cannot overlook the possibility that results were influenced by sex differences.

In summary, we demonstrated that a history of childhood abuse interacts with the low activity MAO-A variant to increase impulsivity in BPD. This result was specific to BPD and adds to a growing literature highlighting the role of G×E effects on the impulsivity of BPD.[65,66] Future studies that test the interaction of childhood abuse and MAO-A expression on borderline symptoms closely related to impulsivity could make important inroads to understanding the etiology and development of BPD. In addition, analyzing the effect of MAO-A genotype and history of childhood abuse on the efficacy of novel treatments for BPD[67] and impulsivity[68] could lead to more targeted interventions for personality disorders.

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