Substance use disorders: Relationship with intermittent explosive disorder and with aggression, anger, and impulsivity

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Abstract

Background—A relationship between substance use and aggression has been noted for decades. While substance use appears to be associated with an increased risk of aggressive behavior, no study has yet reported on the pattern of comorbidity and temporal relationship between impulsive aggression (i.e., intermittent explosive disorder) and substance use disorders (SUD), specifically.

Methods—To specify these relationships, we examined DSM-5 diagnosis data from diagnostic interviews of 1355 adults who met one of five non-overlapping diagnostic subgroups: those with intermittent explosive disorder (IED; n = 339), those with SUD (n = 136), IED+SUD (n = 280), adults with psychiatric disorders but no SUD or IED (n = 320), and healthy Controls: HC, n = 282).

Results—Occurrence of lifetime SUD was elevated in IED *vs.* all Non-IED subjects (Odds Ratio: 3.61 [95% CI: 2.82–4.63]) and onset of IED preceded SUD in 80% of comorbid IED+SUD cases. Examination of the severity of impulsive aggression and SUD revealed that IED increased SUD severity but the presence of SUD did not increase severity of IED core features, including aggression, anger, or impulsivity.

Conclusions—Subjects with IED are at increased risk of developing substance use disorder, compared to those without IED. This suggests that history of recurrent, problematic, impulsive aggression is a risk factor for the later development of SUD rather than the reverse. Thus, effective treatment of impulsive aggression, before the onset of substance misuse, may prevent or delay the development of SUD in young individuals.

Keywords

IED substance use disorder; Aggression; Anger; Impulsivity

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1. Introduction

Intermittent Explosive Disorder (IED) is characterized by recurrent, problematic, impulsive aggressive behavior (Amercian Psychiatric Association, 2013). While it was previously thought that the impulsive aggressive behavior in IED was due to the presence of other psychiatric disorders, data from an early study revealed that IED exists in pure form and is more prevalent than once thought (Felthous et al., 1991). Subsequent epidemiologic data from adults and adolescents indicate that the prevalence of IED is greater than 3–5% and that the age of onset of IED is earlier than that of most other psychiatric disorders (Kessler et al., 2006; McLaughlin et al., 2012). Accordingly, when impulsive aggressive outbursts are not limited to episodes of another psychiatric or medical disorder, the diagnosis of IED may be made. In clinical samples, IED is typically comorbid with other disorders such as depression, anxiety, and substance use, disorders (Coccaro, 2012). While we previously reported on comorbidity issues of IED with depressive and anxiety disorders (Coccaro, 2011; Coccaro et al., 1998), to our knowledge there are no published studies addressing the pattern of comorbidity and temporal aspects of IED and substance use disorders (SUDs). This is important because associative data suggests that substance use/misuse leads to aggressive behavior and that aggressive behavior, in those who use/misuse substances, should be considered secondary to substance use/ misuse.

The relationship between aggressive behavior and SUDs has been addressed in the literature for many years. A variety of substances have been linked to an increase in the risk of aggressive behavior, notably, alcohol, cannabis, cocaine, and amphetamines (Beck et al., 2014; Boles and Miotto, 2003; Hoaken and Stewart, 2003). This statement belies the complexity of such comorbidity. One important issue concerns how aggression is defined. For example, there are at least two forms of aggressive behavior: a) aggressive behavior that is impulsive or reactive/defensive in nature (Barratt et al., 1997a; Cornell et al., 1996; Kockler et al., 2006; Stanford et al., 2003); and b) aggressive behavior that is premeditated and is typically associated with psychopathy (Barratt et al., 1997a; Coccaro et al., 2014; Cornell et al., 1996). The second important issue in understanding this comorbidity is the association between substance use and aggression. Substance use may influence aggressive behavior directly through disinhibitory effects of acute intoxication (McCloskey et al., 2009) or indirectly through social contexts, personality variables, or exposure to violence (Hoaken and Stewart, 2003). Conversely, it is also possible that problematic aggressive behavior increases the risk for substance use/misuse and/or that the two share a similar substrate as the two disorders share similar event related potential anomalies in electroencephalographic studies (Barratt et al., 1997b; Moeller et al., 2004). Accordingly, with the advent of the reliable and valid clinical diagnosis of IED, the categorical expression of impulsive aggression (Coccaro, 2012), it is timely to examine the relationship between IED and SUD.

In this study, we analyzed clinical research data from extensive diagnostic interviews conducted in the context of our larger clinical research program of impulsive aggression in order to examine the relationship between IED and SUD. Subjects with current SUD were not included in these studies because the current comorbid presence of SUD would compromise interpretation of the various psychobiological studies we were conducting. That said, a substantial number of our subjects had a lifetime history of SUD and this allowed us

to examine the extent and nature of the comorbidity between IED and SUD, including patterns of aggression, anger, and impulsivity scores as a function of IED and SUD, as well as the relative ages of onset of IED and SUD in individuals with lifetime diagnoses of both disorders. The latter is particularly important because analysis of age of onset data can help elucidate which disorder appears first in comorbid cases. Based on the literature, and on research experience in working with individuals with recurrent, problematic, impulsive aggressive behavior (McCloskey et al., 2009), we hypothesized that: a) persons with current or past IED would have higher risk of lifetime SUDs compared with non-IED participants; b) persons with comorbid IED + SUD would show earlier age of onset of IED than SUD; c) persons with comorbid IED + SUD would exhibit greater severity of SUD but not the reverse; and, d) dimensional measures of aggression, anger, and impulsivity would be highest in both IED and in IED + SUD subjects compared with all other subjects.

2. Methods

2.1. Subjects

The sample was comprised of 1355 physically healthy adults systematically evaluated in regard to aggression, anger, impulsivity, and other behaviors as part of a clinical research program designed to study behavioral and biological correlates of impulsive aggressive, and other personality-related, behaviors in human subjects. Participants were recruited through public service announcements, newspaper, and other media, advertisements seeking out individuals who: a) reported psychosocial difficulty related to one or more syndromal (formerly Axis I) and/or personality (formerly Axis II), disorders or, b) had little evidence of psychopathology (i.e., healthy controls). All participants gave informed consent and signed the informed consent document approved by the University of Chicago Institutional Review Board (IRB).

2.2. Diagnostic assessment

Syndromal and personality disorder diagnoses were made according to DSM-5 criteria (Amercian Psychiatric Association, 2013). Diagnoses were made using information from: (a) the Structured Clinical Interview for DSM Diagnoses (SCID; First et al., 1995) for syndromal disorders and the Structured Interview for the Diagnosis of DSM Personality Disorder (Pfohl et al., 1997) for personality disorders; (b) clinical interview by a research psychiatrist; and, (c) review of all other available clinical data. The research diagnostic interviews were conducted by individuals with a masters or doctorate degree in clinical psychology. All diagnostic raters completed a rigorous training program that included lectures on DSM diagnoses and rating systems, videos of expert raters conducting SCID/SIDP interviews, and practice interviews and ratings until the raters were deemed reliable with the trainer. This process resulted in good to excellent inter-rater reliabilities (mean kappa of 0.84 ± 0.05; range: 0.79–0.93) across anxiety, mood, substance use (excluding nicotine), impulse control, and personality disorders. Final diagnoses were assigned by team best-estimate consensus procedures as previously described (Coccaro et al., 2014). All participants with a lifetime diagnosis of substance use disorder (SUD) met at least two DSM-5 criteria for SUD (with the exception of the criteria for craving which was not available for participants in this study). As in our previous studies, participants with a

lifetime history of bipolar disorder, schizophrenia (or other psychotic disorder), or mental retardation were excluded from study, as were participants meeting DSM-5 criteria for a current SUD (i.e., participants with a life history of substance use were in a sustained remission of at least 1 year at time of study).

The sample was divided into five subgroups based on DSM-5 diagnosis: a) Healthy Controls (HC; n = 282): Participants with no evidence of current or past psychiatric disorder; b) Psychiatric Controls (PC; n = 320): Participants meeting criteria for a current or lifetime psychiatric disorder but not lifetime diagnosis of either IED or SUD; c) Substance Use Disorder (SUD; n = 136): Participants meeting DSM-5 criteria for at least one SUD lifetime but not IED; d) Intermittent Explosive Disorder (IED; n = 339): Participants meeting criteria for IED but not lifetime SUD; and, e) IED + SUD (n = 280): Participants meeting criteria for current or lifetime diagnosis of IED and a lifetime diagnosis of SUD. For participants with any psychiatric diagnosis (n = 1073), most (70.4%) reported: a) history of formal psychiatric evaluation and/or treatment (57.1%) or, b) history of behavioral disturbance during which the subject, or others, thought they should have sought mental health services but did not (13.3%). Table 1 displays the diagnostic data for each of the five study groups.

2.3. Measures of trait aggression, anger, impulsivity

Aggression was assessed with the Aggression score from the Life History of Aggression (LHA; Coccaro et al., 1997) assessment and with the Verbal and Physical Aggression scores from the Buss-Perry Aggression Questionnaire (BPAQ; Buss and Perry, 1992). The LHA assesses history of actual aggressive behavior and BPAQ and BPAQ assesses aggressive tendencies as a personality trait. Trait Anger was assessed with the State-Trait Anger and Expression of Anger Inventory (STAXI; Spielberger, 1996) and with the Anger score from the BPAQ. Impulsivity was assessed with the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995) and the Impulsivity Scale from the Eysenck Personality Questionnaire (EPQ-2; Eysenck and Eysenck, 1977). In addition, the Neuroticism, Psychoticism, and Extraversion scales, from the EPQ-1 (Eysenck and Eysenck, 1991), were available as control personality variables.

2.4. Severity of SUD

Severity of SUD was assessed in three ways. First, as per DSM-5 guidelines, severity for each SUD was expressed as "mild" (2–3 SUD criteria met), "moderate" (4–5 SUD criteria met), and "severe" (6 SUD criteria met). In addition, severity was also coded by the number of different SUD diagnoses met and the cumulative total number of DSM-5 diagnostic criteria met across all SUD diagnoses for each participant.

2.5. Statistical analysis and data reduction

Statistical procedures included Chi-square, binary logistic regression, multiple regression, analysis of covariance (ANCOVA), *t*-test, paired *t*-test, and Pearson correlation, as appropriate. All reported odds ratios were adjusted for age, sex, ethnicity, and socioeconomic status. A two-tailed alpha value of 0.05 was used to denote statistical significance for all analyses. Data reduction involved the creation of composite variables for trait aggression, trait anger, and trait impulsivity. Since each of the individual variables

related to these dimensions were highly correlated with each other, composite variables were created by z-transforming each individual variable and taking the mean z-score of each of the related variables.

3. Results

3.1. Characteristics of the sample

The five groups differed significantly in age and socioeconomic class and modestly in the distribution of gender and race. Accordingly, all analyses factored in these demographic differences. In addition, groups differed in scores on all behavioral variables in the expected fashion (Table 2).

3.2. Comorbidity rates for IED and SUD

IED was significantly associated with past history of any SUD; Table 3. This relationship was the same regardless of whether subjects met DSM-5 criteria for current IED-Only [44.8% *vs.* 18.4%; Odds Ratio: 3.55 (95% CI: 2.73–4.61, $p < 0.001$)] or met DSM-5 criteria for IED only in the past [47.9% *vs.* 18.4%; Odds Ratio: 3.98 (95% CI: 2.62–6.06; $p < 0.001$)]. Removing HC subjects from the analysis revealed a significant association between IED and SUD even when the comparison group only included subjects with history of a psychiatric disorder (Table 3).

3.3. Comorbid IED + SUD: comparative age of onset of IED and SUD

Age of onset for first having "problems" due to IED was earlier than that for the age of onset of first having "problems" due to any SUD. In this fashion, IED preceded SUD in 80.1% of cases while SUD preceded IED in only 15.1% of cases; both diagnoses were made in the same year in 4.8% of cases. When IED preceded SUD, age of onset of IED preceded that of SUD by about nine years (mean age of onset = 11.9 ± 4.8 *vs.* 21.2 ± 6.5 years, $t_{232} = 21.79$, $p < 0.001$); when SUD preceded IED, age of onset of SUD preceded that of IED by about five years (16.5 ± 3.6 *vs.* 21.8 ± 6.2 years, $t_{43} = 5.96$, $p < 0.001$). The rate of comorbidity of IED with SUD did not differ whether onset of IED preceded onset of SUD or the reverse.

3.4. Severity of SUD in comorbid IED + SUD

Compared with SUD-only subjects, IED + SUD subjects had greater number of SUD diagnoses (1.7 ± 0.9 *vs.* 1.5 ± 0.8; $t_{300} = 2.48$, $p = 0.014$; $d = 0.22$), as well as greater number of total cumulative DSM-5 SUD criteria met across all SUDs (7.9 ± 5.2 *vs.* 6.6 ± 4.6; $t_{300} = 2.55$, $p = 0.011$; $d = 0.25$).

3.5. Relationship between substance use disorder subtypes and IED

Examination of the frequency of each specific SUD revealed that each substance use disorder (e.g., alcohol, cannabis) was more prevalent in IED subjects than non-IED subjects, although the SUDs did not differ in their rates of comorbidity with IED (see Table 3). Given the comorbidity among substance use disorders, the SUDs were entered into a single model to assess which were uniquely associated with IED. Only alcohol ([Odds Ratio: 2.51 [95% CI: 1.89–3.32], $p < 0.001$) and cannabis (Odds Ratio: 1.85 [95% CI: 1.20–2.85], $p = 0.006$)

use disorders were significantly associated with IED. Stimulant (Odds Ratio: 1.60 [95% CI: 0.98–2.61], p = 0.058) and opioid (Odds Ratio: 3.10 [95% CI: 0.86–11.14], p = 0.083) use disorders were marginally associated with IED. Age of onset of IED was earlier than that for each of the individual substances: alcohol (IED: 13.9 ± 6.4 *vs.* 22.3 ± 7.3 years; t_{243} = 14.42, p < 0.001), cannabis (IED: 13.4 ± 6.1 *vs.* 18.3 ± 4.5 years; t_{118} = 7.02, p < 0.001), stimulant (IED: 14.0 ± 6.2 *vs.* 22.1 ± 6.0 years; t_{88} = 8.62, p < 0.001), and opioid (IED: 12.1 ± 4.0 *vs.* 26.1 ± 7.4 years; t_{17} = 6.01, p < 0.001), use disorders.

3.6. Influence of other psychiatric comorbidity on the relationship between IED and SUD

The association between IED and SUD was not influenced by comorbidity with any other DSM-5 disorder. For all comparisons, odds ratios for the association between IED and SUD, in the presence of each comorbidity, were significant and ranged from 1.78 (95% CI: 1.18–2.69, p = 0.007) to 2.19 (95% CI: 1.48–3.24, p < 0.001).

3.7. Aggression, anger, and impulsivity as a function of subject group (Fig. 1)

In order to explore if the groups differed in trait aggression, anger, and impulsivity, separate ANCOVA analyses with these variables were conducted with age, sex, race, and socioeconomic score as covariates. ANCOVA revealed that Composite Aggression scores differed significantly among the groups (F[4,1346] = 389.29, p < 0.001). Post-hoc analysis revealed that comorbid IED + SUD and IED subjects had significantly higher composite aggression scores than the SUD, PC, and HC groups. The comorbid IED + SUD and IED groups did not differ from each other in mean composite aggression score. ANCOVA of composite anger scores revealed significant differences among the groups (F[4,1023] = 182.91, p < 0.001) with post-hoc analysis mirroring those of composite aggression scores. Likewise, ANCOVA of composite impulsivity scores revealed significant differences among the groups (F[4800] = 64.04, p < 0.001). These results were the same after controlling for: a) substance use severity (i.e., number of DSM-5 SUD diagnostic criteria met across all SUD diagnoses); b) personality measures (EPQ neuroticism, psychoticism, and extraversion scores) and, c) DSM-5 diagnoses that differed among the groups (i.e., lifetime depressive, anxiety, stress-related, and impulse control, disorders as well as personality disorders).

3.8. Dimensional relationship between aggression, anger, and impulsivity and severity of SUD

In addition to categorical relationships among aggression, anger, and impulsivity, across subject groups, each correlated with the number of DSM-5 SUD diagnostic criteria met in each subject (Aggression: r = 0.32, n = 1355, p < 0.001; Anger: r = 0.28, n = 1032, p < 0.001; Impulsivity: r = 0.28, n = 809, p < 0.001). Multiple regression analysis revealed that composite aggression (β = 0.31, p < 0.001) and composite impulsivity (β = 0.12, p = 0.003), but not composite anger (β = 0.01, p = 0.865), scores, significantly predicted the number of DSM-5 SUD criteria met (R^2 = 0.16, F[3767] = 47.33, p < 0.001).

4. Discussion

In this study, the presence of IED was associated with a threefold increased risk of lifetime substance use disorder across all participants. When examined only in participants with a

psychiatric diagnosis, the presence of IED doubled the risk of an SUD. However, these numbers likely underestimate the odds ratio that might be observed in an epidemiologic sample because the comparison group comprised a substantially greater number of subjects with psychiatric disorders, already at elevated risk for SUD, than would be expected in a general population sample. In support of this view, reanalysis of the National Comorbidity Study-Replication (NCS-R) by our group estimates the odds ratio for IED + SUD comorbidity at 5.42 (95% CI: 3.88–7.55; Coccaro et al., in press).

The extent of IED + SUD association was not influenced by current-versus past-status of IED as the odds ratio for subjects with current IED was the same for those who met IED criteria only in the past. While this suggests no state-dependency to the comorbidity of IED with SUD, as a function of IED, our data do not allow us to comment on IED + SUD comorbidity as a function of the current- *vs.* past-status of SUD. This is because our studies were designed to investigate impulsive aggression in the absence of current, though not past, SUD. That said, our NCS-R reanalysis, which looked specifically at the comorbidity of current IED with current SUD, revealed similar findings to the ones reported here (Coccaro et al., in press).

The temporal nature of IED + SUD comorbidity is critical to the understanding of how these two disorders intersect. In this study, age of onset of "problems" due to IED preceded that of "problems" due to SUD in nearly 80% of the comorbid subjects. Prior research has also indicated that IED has an earlier onset, on average (e.g., mid-second decade of life), than substance use disorder (early third decade of life; Kessler et al., 2006). The present study extends these findings to show that, for the majority of individuals with comorbid IED and SUD, problematic impulsive aggressive behavior was not due to the onset of SUD. Thus, IED may represent a risk factor for later SUD, rather than the reverse, and that intervention designed to treat impulsive aggression at an early age may reduce the later onset of SUD.

Among SUD subtypes, these data support a significant association between IED and alcohol, cannabis, and possibly stimulant and opioid, use disorders. Intoxication with alcohol has long been known to increase the risk of aggressive behavior, especially in those with high trait aggression. On the other hand, cannabis intoxication is associated with a reduction in aggressive behavior, while cannabis withdrawal in heavy cannabis users is associated with a withdrawal syndrome associated with increases in irritability and other behavioral symptoms (Budney et al., 2003; Kouri and Pope, 2000; Kouri et al., 1999). In addition, many cannabis using subjects report that they use cannabis to "treat" irritability and aggressive urges (Arendt et al., 2007).

Examining subjects as a function of diagnostic group revealed no significant differences between IED + SUD and IED-Only subjects in ratings of aggression, anger, and impulsivity suggesting that the presence of SUD does not enhance the severity of these behavioral dimensions. In addition, adding SUD severity to the statistical models did not change this result indicating that similar levels of aggression, anger, and impulsivity between IED + SUD and IED-Only subjects were not related to differences in the severity of SUD. That said, these data also show that aggression, anger, and impulsivity scores were significantly higher in SUD-Only, compared with PC (and HC), subjects. This indicates that the presence

of SUD, even in the absence of an IED diagnosis, is associated with greater aggression, anger, and impulsivity compared with comparable (and healthy), subjects. Close examination of aggression scores, for example, reveals that while mean LHA Aggression scores of SUD-Only subjects were higher than those of PC subjects, two-thirds of these subjects had LHA Aggression scores below the lower range of clinically meaningful aggression (i.e., 12–25 for LHA Aggression) underscoring that while more aggressive, SUD-Only subjects were not particularly "aggressive".

In contrast, severity of SUD, as assessed in this study, appears to be greater in IED + SUD, compared with SUD-Only, subjects. This suggests that the presence of IED enhances the severity of substance use. Not surprisingly, there was a positive correlation between SUD severity and aggression, anger, and impulsivity scores. Follow-up analysis revealed that aggression and impulsivity scores uniquely predicted SUD severity with the β value for aggression as nearly three times, and the degree of variance explained as nearly seven times (i.e., 6.67), as high as that for impulsivity; the relationship between anger and SUD severity was completely accounted for by its covariance with aggression and impulsivity.

This study has several strengths and limitations. Its greatest strength is the large clinical sample in which psychiatric diagnoses were assessed systematically with psychometrically valid and reliable measures of aggression, anger, and impulsivity. Limitations include the cross-sectional nature of this study, the exclusion of persons with current SUD, and that participants were recruited from a clinical research center and did not also include those recruited from treatment facilities. As a cross-sectional study, associations reported cannot be translated into causation. That said, the observation that age of onset of the diagnosis of IED preceded that of the diagnosis of SUD in 80% of subjects strongly suggests that SUD was not the "cause" of IED in the vast majority of subjects. Current SUD was not studied because the aim of the overall study was to investigate impulsive aggression in the absence of various factors (e.g., psychosis, bipolar mood disorder), including substances that could affect aggression; this left only past SUD in the sample. While the psychiatric subjects in the study were not primarily recruited from treatment settings, 70% had history of formal treatment for psychiatric disorder (57%) or of behavioral disturbance that should have been assessed by mental health professionals (13%). Accordingly, most of the psychiatric subjects in this study should be similar to those drawn from a treatment setting.

5. Conclusion

Comorbidity of IED with SUD, in this clinical research sample, was common and substantial in numbers with an elevated odds ratio of 3.61. In addition, onset of IED preceded that of SUD in 80% of comorbid cases suggesting that IED increases the risk of SUD, rather than the reverse, in the vast majority of comorbid cases. In support of this we found that the presence of IED was associated with increased severity of SUD while the presence of SUD was not associated with increased severity of impulsive aggression. Given these data, effective treatment of impulsive aggression, after the onset of IED but before the onset of substance misuse, may prevent, or delay, the development of SUD in young individuals.

Acknowledgments

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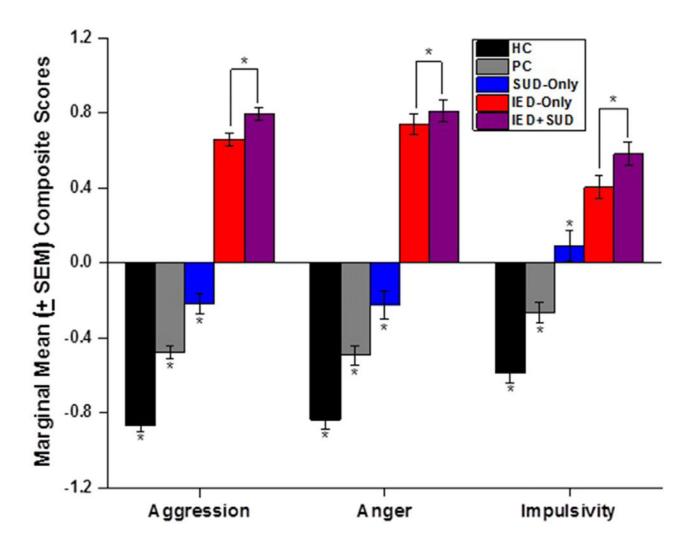
Fig. 1.
Marginal mean (±sem) composite scores of trait aggression, trait anger, and trait impulsivity in the groups (all scores after ANCOVA with age, sex, race, and socioeconomic score as covariates).

Table 1

DSM-5 syndromal and personality disorders in the sample.

	PC (N = 320)	SUD only (N = 136)	IED only (N = 339)	IED + SUD (N = 280)	p=
Current syndromal disorders:					
Any depressive mood disorder	42 (13.1%)	22 (16.2%)	72 (21.4%)	72 (25.7%)	<0.001 *
Any anxiety disorder	28 (8.8%)	23 (16.9%)	68 (20.2%)	64 (22.9%)	<0.001 *
Obsessive-compulsive disorders	2 (0.6%)	1 (0.7%)	11 (3.3%)	7 (2.5%)	=0.027
Traumatic and stress disorders	6 (1.9%)	5 (3.7%)	18 (5.3%)	28 (10.0%)	<0.001 *
Impulse control disorders (Not-IED)	3 (0.9%)	4 (2.9%)	8 (2.4%)	11 (3.9%)	=0.027
Eating disorder	5 (1.6%)	2 (1.5%)	13 (3.9%)	14 (5.0%)	=0.008
Somatoform disorder	4 (1.3%)	0 (0.0%)	12 (3.6%)	2 (0.7%)	=0.637
Lifetime syndromal disorders:					
Any depressive mood disorder	127 (39.7%)	62 (45.6%)	190 (56.4%)	194 (69.3%)	<0.001 *
Any anxiety disorder	47 (14.7%)	30 (21.1%)	84 (24.9%)	87 (31.1%)	<0.001 *
Obsessive-compulsive disorders	4 (1.3%)	3 (2.2%)	12 (3.6%)	10 (3.6%)	=0.046
Traumatic and stress disorders	11 (3.4%)	12 (8.8%)	28 (8.3%)	44 (15.7%)	<0.001 *
Impulse control disorders (Not-IED)	8 (2.5%)	7 (5.1%)	17 (5.0%)	25 (8.9%)	<0.001 *
Eating disorder	18 (5.6%)	9 (6.6%)	24 (7.1%)	29 (10.4%)	=0.037
Somatoform disorder	4 (1.3%)	0 (0.0%)	13 (3.9%)	2 (0.7%)	=0.582
Personality disorders:					
Cluster A (Odd)	27 (8.4%)	13 (9.6%)	47 (13.9%)	55 (19.6%)	<0.001 *
Cluster B (Dramatic)	41 (12.8%)	37 (27.2%)	113 (33.5%)	156 (55.7%)	<0.001 *
Cluster C (Anxious)	56 (17.5%)	18 (13.2%)	79 (23.4%)	74 (26.4%)	=0.002
PD-NOS	98 (30.6%)	36 (26.5%)	138 (40.9%)	67 (23.9%)	=0.641

*
Significant for linear by linear association after correction for multiple comparisons (p < 0.002).

**
Significant for Pearson X^2 (df = 3) after correction for multiple comparisons (p < 0.002).

Table 2

Demographic and behavioral characteristics of sample.

	HC (N = 282)	PC (N = 320)	SUD (N = 136)	IED (N = 339)	IED/SUD (N = 280)	p=	Group differences
Demographic variables							
Age[a] (Years)	31.9 ± 11.5	34.6 ± 11.8	36.0 ± 10.3	35.9 ± 10.7	37.3 ± 9.5	<0.001	IED + SUD > PC = HC IED + SUD = IED = SUD
Gender[b] (%: M/F)	55/45	54/46	61/39	54/46	66/44	=0.018	For % male: IED + SUD > HC = PC = IED IED + SUD = SUD
Race[b] (%: W/AA/Other)	60/26/14	56/37/7	60/31/9	55/33/12	62/31/7	=0.013	For % AA: HC < PC IED + SUD = SUD = IED
SES score[a]	39.6 ± 13.5	34.7 ± 13.5	33.3 ± 13.6	37.8 ± 12.6	37.2 ± 12.3	<0.001	HC = IED HC > PC = SUD = IED + SUD
Behavioral variables							
GAF score[c]	84.1 ± 5.3	66.9 ± 11.9	63.9 ± 12.8	57.0 ± 8.4	54.4 ± 8.5	<0.001	HC > PC > SUD > IED = IED + SUD
LHA trait aggression[c]	4.8 ± 3.6	7.7 ± 5.2	9.6 ± 5.6	17.4 ± 4.8	18.2 ± 4.7	<0.001	IED + SUD = IED > SUD > PC > HC
Buss trait aggression[c]	26.2 ± 10.1	31.1 ± 10.9	35.3 ± 10.9	44.7 ± 12.7	47.7 ± 11.9	<0.001	IED + SUD = IED > SUD > PC > HC
Buss trait anger[c]	8.1 ± 7.9	11.3 ± 9.8	13.8 ± 10.2	23.6 ± 8.5	24.6 ± 8.7	<0.001	IED + SUD = IED > SUD > PC > HC
Spielberger trait anger[c]	13.7 ± 3.0	16.6 ± 5.9	17.9 ± 5.5	25.0 ± 7.3	25.3 ± 8.0	<0.001	IED + SUD = IED > SUD > PC > HC
BIS-11 Trait Impulsivity[c]	55.6 ± 9.0	60.8 ± 10.6	64.5 ± 9.2	67.7 ± 11.8	70.2 ± 11.5	<0.001	IED + SUD = IED = SUD > PC > HC
EPQ-2 trait impulsivity[c]	3.5 ± 3.4	4.7 ± 3.7	6.4 ± 4.3	7.3 ± 4.4	8.5 ± 4.7	<0.001	IED + SUD = IED > SUD > PC > HC

[a]
p by ANOVA.

[b]
p by Chi-Square.

[c]
p by ANCOVA (age, sex, race, SES score as covariates).

Table 3

Lifetime substance use disorders as a function of IED.

	IED+ (N = 617)	IED- (N = 738)	Adjusted odds ratio (95% CI) all subjects	Adjusted odds ratio (95% CI) psychiatric subjects only[a]
Any substance use disorder	280 (45.4%)	136 (8.4%)	3.61 (2.82–4.63)[b]	1.99 (1.53–2.58)[b]
Alcohol use disorder	226 (36.6%)	112 (15.2%)	3.16 (2.43–4.11)[b]	1.79 (1.36–2.35)[b]
Cannabis use disorder	107 (17.3%)	42 (5.7%)	3.39 (2.32–4.95)[b]	2.10 (1.43–3.09)[b]
Stimulant use disorder	90 (14.6%)	33 (4.5%)	3.46 (2.27–5.26)[b]	2.23 (1.46–3.41)[b]
Opioid use disorder	18 (2.9%)	3 (0.4%)	6.03 (1.76–20.69)[b]	4.15 (1.20–14.29)
Hallucinogen use disorder	14 (2.3%)	6 (0.8%)	2.96 (1.12–7.79)	1.96 (0.74–5.18)
Sedative-hypnotic use disorder	9 (1.5%)	1 (0.1%)	11.05 (1.39–8.09)	7.46 (0.94–58.82)
Multiple drug use disorder	9 (1.5%)	3 (0.4%)	3.23 (0.87–12.07)	2.18 (0.58–8.13)

[a]Excludes Healthy Control subjects and represents the Adjusted Odds Ratio for IED (n = 617) and SUD versus all other DSM-5 disorders (n = 456) in the study.

[b]Significant for binary logistic regression after correction for multiple comparisons (p 0.006).