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Relationship Between Psychopathy, Aggression, Anger, Impulsivity, and Intermittent Explosive Disorder

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Intermittent explosive disorder (IED) in DSM-5 represents a disorder of recurrent, problematic, reactive (i.e., affective or impulsive), aggressive behavior that, over the lifetime, affects about 5–6% of individuals in the United States. While aggression is also observed in those with psychopathic personality, aggression in this context is frequently proactive rather than reactive, and neurobiological study suggests important differences between those with proactive aggression/psychopathy and those with reactive aggression. In this paper, we conducted two sets of analyses. First, a phenomenologic study to explore the frequency of psychopathic personality defined by the Psychopathology Checklist-Screening Version (PCL-SV) among IED and comparator participants and to explore differences in measures of aggression, anger, and impulsivity as a function of IED and psychopathic personality. Second, we re-analyzed data from five published studies to determine if psychopathic personality accounted for differences between IED and comparator participants. The first study found that only a modest proportion of IED participants display clinically substantial features of psychopathy and that measures of trait aggression and anger, rather than those of psychopathy, are the strongest correlates of IED. The second study found little evidence for any impact of psychopathy on reported findings in IED compared with various control participants. Aggr. Behav. 9999:XX–XX, 2014. © 2014 Wiley Periodicals, Inc.

Keywords: IED; aggression; anger; impulsivity; psychopathy

INTRODUCTION

Human aggression constitutes a multi-determined verbal and/or physical act that results in physical/psychological injury to others and/or destruction of property/other objects (Coccaro, 2012). It appears in several forms and may be proactive (i.e., "premeditated" or "predatory") or reactive (i.e., "affective" or "impulsive") in nature (Dodge, Lochman, Harnish, Bates, & Pettit, 1997). Specific acts of aggression may be situational, but the tendency to behave aggressively represents a behavioral trait. While the frequency of aggressive acts tends to decrease with advancing age, numerous studies document that the trait of aggressiveness begins early in life and continues through adulthood (Olweus, 1979).

Both forms of aggression (i.e., proactive and reactive) have the potential for significant physical and psychological harm to the individual, to those subjected to its effects and to society in general. However, in addition to the obvious descriptive differences between the two, both forms of aggression differ in important ways. For example, individuals with psychopathy, who often display proactive aggression, are reported to have attenuated corticolimbic brain responses to emotionally relevant stimuli (Dolan & Fullam, 2009; Harenski, Harenski, Shane, & Kiehl, 2010; Müller et al., 2008; Pujol et al., 2012; Rilling et al., 2007). In contrast, non-psychopaths, who typically display reactive aggression, are reported to have enhanced responses to anger faces in the amygdala and attenuated responses in the orbitomedial prefrontal cortex (Coccaro, McCloskey, Fitzgerald, & Phan, 2007). In addition, other empirical data

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consistently link reactive aggression to specific biological (Linnoila et al., 1983; Raine et al., 1998), social–emotional information processing (Dodge, Pettit, & Bates, 1994), and pharmacological (Barratt, Stanford, Felthous, & Kent, 1997; Sheard, Marini, Bridges, & Wagner, 1976) treatment response factors when compared with the proactive aggression seen in psychopaths.

The diagnostic entry in the DSM-5 that best describes recurrent, reactive aggression is intermittent explosive disorder (IED). Based on DSM-IV criteria, rates of IED in the United States. for lifetime, and past year, are in the range of about 5–6%, and 2–3%, respectively (Kessler et al., 2006). However, because DSM-5 criteria for IED allow for "high frequency/low intensity," as well the "low frequency/high intensity" outbursts described in DSM-IV, these rates may underestimate the actual prevalence of DSM-5 IED in the United States by as much as 20% (Coccaro, Schmidt, Samuels, & Nestadt, 2004).

Compared with appropriate control participants, IED has been associated with a number of findings. These include an increased rate of IED in first degree relatives of IED probands (Coccaro, 2010), reductions in physiological responses to serotonergic stimulation (Coccaro, Lee, & Kavoussi, 2010a), reductions in the number of platelet serotonin transporter binding sites (Coccaro, Lee, & Kavoussi, 2010b), and treatment response to serotonin selective uptake inhibitors (SSRIs; Coccaro, Lee, & Kavoussi, 2009) and to anger-based cognitive behavioral treatment interventions (McCloskey, Noblett, Deffenbacher, Gollan, & Coccaro, 2008).

An important variable not discussed, to date, is the role of psychopathic personality in IED and with respect to aggression, anger, and impulsivity. The presence of aggression in psychopathic personality has long been known and often thought to be generally proactive in nature. However, while DSM-5 IED Criteria requires its aggressive outbursts to be impulsive, and/or anger-based (i.e., reactive), psychopaths can display aggression in both its proactive and reactive forms. Thus, it is an open question as to how psychopathy interacts with IED as now codified in DSM-5.

Current views of psychopathy have focused on two, if not more, factors (Blair, 2006; Kiehl, 2006): first, a "callous/unemotional" factor including superficial emotionality, grandiosity, lack of remorse, lack of empathy, deceitfulness, and denial of responsibility; second a "social deviant" factor including childhood/adolescent antisocial behavior, adult antisocial behavior, impulsivity, lack of clear goals, lack of behavioral controls, and irresponsibility. Of the two, the former has emerged as a critical factor underlying many of the important features of psychopathy, especially in regard to brain structure and function. Recent research has documented psychopaths to display attenuated corticolimbic responses to emotionally relevant stimuli in the prefrontal, orbitofrontal cortex, and in the amygdala. Specifically, studies of psychopaths demonstrate lower fMRI blood oxygen level dependent (BOLD) prefrontal cortex responses in emotional integration tasks (Müller et al., 2008), moral-reasoning tasks (Pujol et al., 2012) and lower fMRI BOLD orbitofrontal cortex responses in cooperation tasks (Rilling et al., 2007), and passive-avoidance tasks (Finger et al., 2011). This is consistent with findings of a reduction in PFC grey matter (Boccardi et al., 2011; de Oliveira-Souza et al., 2008; Tiihonen et al., 2008). Similarly, psychopaths demonstrate an attenuated fMRI BOLD amygdala response to fear faces (Dolan & Fullam, 2009), moral violations (Harenski et al., 2010), and passive-avoidance learning (Finger et al., 2011). Thus, current models of psychopathy proposed by Kiehl (2006) and by Blair (2006) suggest that such findings are more specifically associated with the presence of "callous/unemotional traits" (the core of "psychopathy" posited by Cleckley, 1988) rather than "social deviance" (i.e., antisocial behavior and lifestyle).

In this paper, we present analyses from two sets of data. The first is a phenomenologic study of over one-thousand individuals in which healthy control, psychiatric control, and IED participants are examined in regards to the presence of psychopathic personality traits and in regards to trait measures of aggression, anger, and impulsivity. The objective of this study was to assess the rate of psychopathic personality in IED compared with control groups engaged in research studies and to explore the relationship between psychopathy and related behavioral variables. We predicted that some degree of psychopathy would be present in the IED, compared with control, participants but that the magnitude of psychopathy would be relatively low and that IED would be more powerfully related to aggression and anger rather than psychopathy of the "callous/unemotional" type. The second data set represents a re-analysis of five published studies, in which we demonstrated that IED can be differentiated from comparator participants in a number of important ways, and to determine if the presence of psychopathic personality, either as a categorical or as a dimensional variable, accounts for reported findings in IED participants. While such data was available at the time of these publications, the results of such analyses were not included in the published papers; given the context of this paper, it is now appropriate to report these analyses in this paper. In this set of analyses, we predicted that psychopathy would play little, if any role, in the selected variables that distinguish IED from control participants.

METHODS

Study I: Relationships Among Psychopathic Personality and Aggression, Anger, and Impulsivity

Subjects. One thousand fifty three physically healthy participants participated in this study (mean age: 33.7 ± 9.6 years; sex: 57.5% men; ethnicity: 56.7% White, 33.2% African-American, 10.1% other; mean Hollingshead SES score: 36.0 ± 13.4). All participants were medically healthy and were systematically evaluated in regard to aggressive, anxiety, and other behaviors as part of a larger program designed to study correlates of impulsive aggressive, and other personality-related, behaviors in human subjects. Subjects were recruited through public service announcements, newspaper, and other media advertisements seeking out individuals who: (a) reported psychosocial difficulties related to one or more Axis I and Axis II conditions or, (b) had little evidence of psychopathology. All participants gave informed consent and signed the informed consent document approved by the Institutional Review Board (IRB).

Assessment of Axis I/II diagnoses and psychopathic personality. Axis I Disorder and Axis II Personality Disorder diagnoses were made according to DSM-IV criteria (APA, 2004). The diagnosis of IED was made by Research Criteria (Coccaro, 2011, 2012). All IED participants also met the new DSM-5 criteria for IED (APA, 2013). Diagnoses were made using information from: (a) the Structured Clinical Interview for DSM Diagnoses (SCID-I) (First, Spitzer, Gibbon, & Williams, 1997) for Axis I disorders and the Structured Interview for the Diagnosis of DSM Personality Disorder (SIDP) (Pfohl, Blum, & Zimmerman, 1997) for Axis II disorders; (b) clinical interview by a research psychiatrist; and, (c) review of all other available clinical/informant data. Research assessment interviews were conducted by individuals with a masters, or doctorate, degree in Clinical Psychology. All diagnostic raters went through a rigorous training program that included lectures on psychiatric diagnoses and rating systems, videos of expert raters conducting the various interviews, and practice interviews and ratings until the rater was deemed reliable. This process resulted in good to excellent inter-rater reliabilities (mean kappa of .84 ± .05; range: .79–.93) across anxiety, mood, substance use, impulse control, and personality disorder. Final DSM-IV diagnoses were assigned by team best-estimate consensus procedures (Klein, Ouimette, Kelly, Ferro, & Riso, 1994; Leckman, Sholomskas, Thompson, Belanger, & Weissman, 1982) involving research psychiatrists and clinical psychologists as previously described (Coccaro, Nayyar, & McCloskey, 2012). This methodology has previously been shown to enhance the accuracy of diagnosis over direct interview alone (Kosten & Rounsaville, 1992). Participants with a life history of bipolar disorder, schizophrenia (or other psychotic disorder), or mental retardation were excluded from this study.

Psychopathic personality was assessed using the Screening Version of the Psychopathy Checklist (PCL-SV) (Hart, Cox, & Hare, 2003) and scored in the context of the diagnostic assessment phase described previously. The PCL-SV is designed to assess for the presence of psychopathic personality in clinical and non-forensic populations. It has separate scores for "callous/unemotional" (Part 1), and for "socially deviant" (Part 2), features of psychopathy. Callous/unemotional psychopathic features relate to "superficial emotionality," "grandiosity," "lack of remorse," "lack of empathy," "deceitfulness," and "denial of responsibility." Socially deviant psychopathic traits relate to "childhood/adolescent antisocial behavior," "adult antisocial behavior," "impulsivity," "lack of clear goals," "lack of behavioral controls," and "general irresponsibility." Total PCL-SV scores range from 0 to 24. Total scores $\leq$12 suggest the absence of psychopathic personality while scores from 13 to 17 suggest possible presence. Scores from 18 to 24 indicate the high likelihood of psychopathic personality. Total callous/unemotional and socially deviant trait scores each range from 0 to 12; scores from 5 to 8 for either type of sub-score suggest the possible presence of these specific psychopathic traits, while scores from 9 to 12 indicate the high likelihood of these specific psychopathic traits.

A total of 252 participants had no evidence of any DSM-IV Axis I or II disorder (healthy controls: HC); 337 participants met criteria for an Axis I and/or II disorder but not for a lifetime diagnosis of either IED or of "possible"/"highly likely" psychopathic personality (psychiatric controls: PC); 354 subjects met criteria for IED but not for "possible"/"highly likely" psychopathic personality (IED); 90 subjects met criteria for IED and "possible"/"highly likely" psychopathic personality (IED/PP), and 20 subjects met PCL-SV criteria for "possible"/"highly likely" psychopathic personality but not for IED (PP).

Among the 337 PC participants, lifetime Axis I disorders were as follows: Any Depressive Mood Disorder ($n = 127$); Any Anxiety Disorder ($n = 59$); Alcohol Dependence ($n = 55$), Other Drug Dependence ($n = 37$), Non-IED Impulse Control Disorder ($n = 8$); Eating Disorder ($n = 18$); Somatoform Disorder ($n = 3$); Adjustment Disorder ($n = 23$). One hundred fifteen PC participants met criteria for a specific Axis II Disorder that belonged to Cluster A ($n = 26$), Cluster B ($n = 52$), or Cluster C ($n = 58$). The remaining 109 of PC

participants with an Axis II disorder were diagnosed with Personality Disorder-Not Otherwise Specified (PD-NOS) (Coccaro et al., 2012). Among the 354 IED participants, Non-IED lifetime Axis I disorders were as follows: Any Depressive Mood Disorder ($n = 225$); Any Anxiety Disorder ($n = 135$); Alcohol Dependence ($n = 90$); Other Drug Dependence ($n = 79$); Non-IED Impulse Control Disorder ($n = 12$); Eating Disorder ($n = 29$); Somatoform Disorder ($n = 9$); Adjustment Disorder ($n = 21$). Two-hundred-eleven of these IED participants met criteria for a specific Axis II Disorder that belonged to Cluster A ($n = 52$), Cluster B ($n = 141$), or Cluster C ($n = 89$). The remaining 124 (38.7%) of IED participants with an Axis II Disorder were diagnosed with PD-NOS. Among the 90 IED/PP participants, Non-IED lifetime Axis I disorders were as follows: Any Depressive Mood Disorder ($n = 63$); Any Anxiety Disorder ($n = 43$); Alcohol Dependence ($n = 44$); Other Drug Dependence ($n = 36$); Non-IED Impulse Control Disorder ($n = 16$); Eating Disorder ($n = 9$); Somatoform Disorder ($n = 3$); Adjustment Disorder ($n = 2$). All but one IED/PP participant met criteria for a specific Axis II Disorder that belonged to Cluster A ($n = 38$), Cluster B ($n = 86$), or Cluster C ($n = 29$). The remaining IED/PP participant was diagnosed with PD-NOS. Among the 20 PP participants lifetime Axis I disorders ($n = 18$) were as follows: Any Depressive Mood Disorder ($n = 10$); Any Anxiety Disorder ($n = 6$); Alcohol Dependence ($n = 5$); Other Drug Dependence ($n = 9$); Non-IED Impulse Control Disorder ($n = 5$); Eating Disorder ($n = 2$); Somatoform Disorder ($n = 1$); Adjustment Disorder ($n = 2$). Nineteen of these PP participants met criteria for a specific Axis II Disorder belonging to Cluster A ($n = 7$), Cluster B ($n = 19$), or Cluster C ($n = 4$). The remaining PP participant was diagnosed with PD-NOS.

Psychometric measures relevant to aggression, anger, impulsivity, and related behavioral dimensions. Aggression was assessed by the Aggression scale from the life history of aggression (LHA) (Coccaro, Berman, & Kavoussi, 1997) and from the Buss-Perry Aggression Questionnaire (BPAQ; Verbal Aggression and Physical Aggression subscales: Buss & Perry, 1992). LHA Aggression assesses the number of times a person has engaged in aggressive behavior while BPAQ Aggression assesses a person's tendency to act aggressively as a personality trait. Anger was assessed by the Anger subscale of the BPAQ and the Trait Anger scale from the State-Trait Anger and Expression of Anger Inventory (STAXI [Spielberger, 1999]). Each measure assesses anger as a personality trait. Impulsivity was assessed by the Life History of Impulsive Behavior (LHIB [Coccaro & Schmidt-Kaplan, 2012]) and Barratt Impulsivity Scale (BIS-11 [Patton, Stanford, & Barratt, 1995]). The LHIB assesses the number of times a person has engaged in impulsive behavior while the BIS-11 assesses the person's tendency to act impulsively as a personality trait. Data for these core dimensions were available on 1,058 for aggression, 816 for anger, and 775 for impulsivity. Global psychosocial functioning of subjects was assessed by the Global Assessment of Function scale (GAF [APA, 1994]) with higher GAF scores reflecting greater psychosocial function.

Statistical analysis. Comparisons of between-group variables were performed by X^2, Fisher's exact test (FET), univariate analysis of variance/covariance (ANOVA/ANCOVA) and multivariate analysis of variance/covariance (MANOVA/MANCOVA) followed by Tukey HSD post-hoc testing. Correlational analyses included Pearson correlation, partial correlation, and multiple regression. A two-tailed alpha value of .05 was used to denote statistical significance for all analyses. Standard deviation (SD), and standard error (SE), of the mean were used in the text and figures, respectively. For purposes of data reduction, composite scores were calculated for Aggression, Anger, and Impulsivity. As previously described (Coccaro et al., 2010b), this was achieved by converting the raw score of each source score (e.g., LHA Aggression + BPAQ Aggression) to a z-score, taking the sum of the z-scores, and dividing by the number of source assessments.

Results

Demographic characteristics of the sample (Table I). HC, PC, PP, IED, and IED/PP participants did not differ in distribution of sex or ethnicity but did differ in age and in Hollingshead socioeconomic class score. The age difference was due to greater age among IED and IED/PP participants than HC and PP participants. The difference in SES Class score was due higher scores among HC and IED participants, middle range scores for PC, and IED/PP subjects and the lowest scores among PP participants. Despite these demographic differences among the groups, multiple regression analysis ($F[4, 1{,}048] = 11.50$, $P < .001$) revealed these four demographic variables explained only 4% of the variance in PCL-SV scores ($R = .20$, $R^2 = .04$) and adding these variables to the statistical models did not change any of the results reported next (Table I).

Prevalence of psychopathic personality among participants. By definition, "psychopathic personality" could only be present in the groups composed of psychiatric participants (i.e., PC and IED, regardless of psychopathy). Among IED participants, about one-fifth met PCL-SV criteria for "possible" or "highly likely" psychopathic personality. This was significantly greater than the rate of psychopathic personality among PC participants (see Fig. 1). The rate of the callous/

TABLE I. Demographic, Functional, and Behavioral Characteristics of Sample

	HC ($N=252$)	PC ($N=337$)	PP ($N=20$)	IED ($N=354$)	IED/PP ($N=90$)	*P*-Value	Group Differences
Demographic variables							
Age	30.4 ± 8.5	33.7 ± 9.6	31.6 ± 7.6	36.0 ± 9.7	34.5 ± 10.5	<.001	HC = PC = PP = IED/PP IED > PP
Gender (M/F)	139/113	205/132	13/7	198/156	51/39	.568	No differences
Race (W/AA/other)	154/67/31	186/130/21	7/9/4	214/107/33	36/37/17	.101	No differences
SES score	38.3 ± 13.6	33.7 ± 13.7	30.6 ± 12.8	37.0 ± 12.9	34.8 ± 12.6	<.001	HC = IED = IED/PP = PC; HC = IED > PP
Psychosocial function							
GAF score	84.0 ± 5.5	66.2 ± 12.1	55.5 ± 10.0	55.7 ± 7.8	50.7 ± 8.5	<.001	HC > PC > PP = IED IED > IED/PP
PCL-SV scores							
Total score	0.6 ± 1.1	3.4 ± 3.3	15.4 ± 2.1	5.9 ± 3.2	16.2 ± 2.5	<.001	HC < PC < IED < PP PP = IED/PP
Part 1 score	0.4 ± 0.8	1.4 ± 1.8	7.7 ± 2.2	1.9 ± 1.8	6.9 ± 2.3	<.001	HC < PC = IED < PP PP = IED/PP
Part 2 score	0.3 ± 0.7	2.0 ± 2.3	7.8 ± 2.7	4.1 ± 2.4	9.3 ± 2.1	<.001	HC < PC < IED < PP PP < IED/PP
Aggression scores							
LHA	4.9 ± 3.8	8.3 ± 5.6	13.0 ± 6.0	17.6 ± 4.7	20.3 ± 3.9	<.001	HC < PC < PP < IED < IED/PP
BPA	28.4 ± 9.6	34.4 ± 10.7	42.6 ± 10.3	47.4 ± 11.6	52.3 ± 11.1	<.001	HC < PC < PP = IED; IED = IED/PP
Anger scores							
BPA	13.1 ± 5.1	16.4 ± 7.0	19.2 ± 6.7	25.8 ± 6.4	27.2 ± 6.7	<.001	HC = PC = PP PP < IED = IED/PP
STAXI	13.6 ± 3.0	17.3 ± 6.5	20.6 ± 3.8	25.9 ± 7.4	30.8 ± 5.4	<.001	HC = PC = PP PP < IED = IED/PP
Impulsivity scores							
LHIB	61.6 ± 37.8	87.4 ± 46.3	177.3 ± 46.0	123.3 ± 41.4	153.0 ± 38.6	<.001	HC = PC < IED < PP PP = IED/PP
BIS-11	55.5 ± 8.8	62.1 ± 10.5	64.5 ± 9.6	68.1 ± 10.9	76.2 ± 11.7	<.001	HC < PC = PP PP = IED < IED/PP

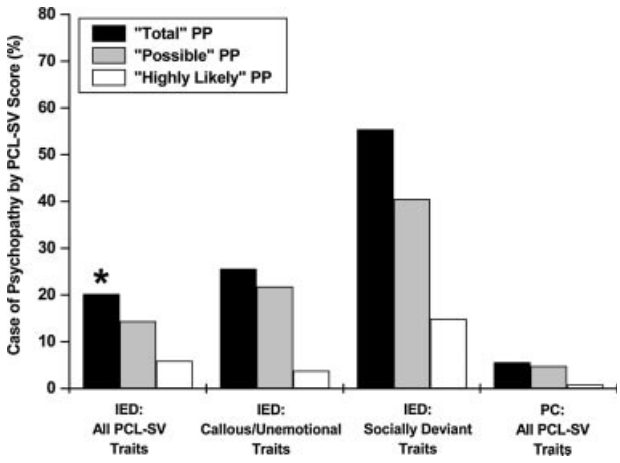

Fig. 1. Percent of IED participants meeting PCL-SV criteria for "Possible" Psychopathy ("Possible" PP), "Highly Likely" Psychopathy ("Highly Likely" PP), and all Psychopathy Cases ("Total" PP) for All PCL-SV traits (IED and PC participants), Callous/Unemotional PP Traits, Socially Deviant PP Traits. Asterisk indicates $P<.05$ total psychopathic traits in intermittent explosive disorder (IED) compared with psychiatric control (PC) participants.

unemotional form of psychopathy, in IED participants, was approximately one-quarter of all cases with only one-fifth of cases coming from the "highly likely" psychopathic group, while the rate of the socially deviant form of psychopathy was noted for more than half of all cases, but with only one-fourth of cases coming from the "highly likely" psychopathic group (see Fig. 1).

Aggression, anger, and impulsivity scores as a function of diagnostic group based on PCL-SV total score. The next set of analyses were performed to examine the association of PCL-SV defined psychopathic personality on core psychometric measures reflecting aggression, anger, and impulsivity. ANOVA revealed significant differences among the groups for each of the composite variables (Composite Aggression: $F[4, 1{,}048] = 340.19$, $P<.001$, HC < PC < PP < IED < IED/PP by Tukey HSD; Composite Anger: $F[4, 811] = 209.02$, $P<.001$, HC < PC = PP < IED = IED/PP; Composite Impulsivity ($F[4, 770] = 76.75$, $P<.001$), HC < PC < PP = IED < IED/PP; see Fig. 2). Adding the demographic variables to the ANCOVA models did not change these results.

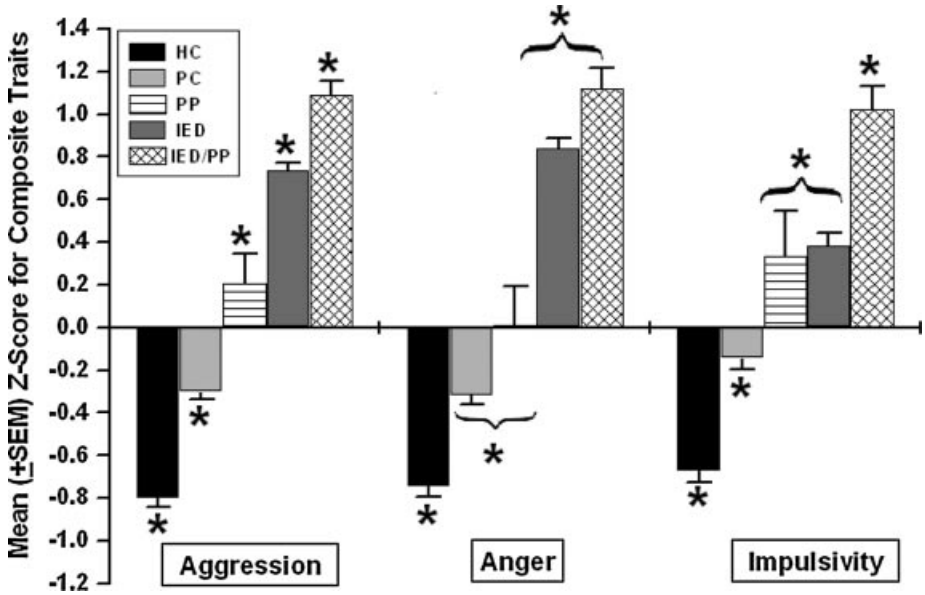

Fig. 2. Mean (±SEM) Composite scores for trait aggression, trait anger, and trait impulsivity in healthy controls (HC), psychiatric controls (PC), psychopathic personality (PP; as defined in the text), intermittent explosive disorder (IED), and IED with psychopathic personality (IED/PP). Asterisk indicates $P < .05$.

Aggression, anger, and impulsivity scores as a function of diagnostic group based on PCL-SV sub-score. ANOVA analysis of the subject groups, as a function of PCL-SV callous/unemotional trait scores, revealed similar differences for the composite variables (Composite Aggression: $F[4, 1{,}048] = 336.69$, $P < .001$, HC < PC < PP < IED < IED/PP by Tukey HSD; Composite Anger: $F[4, 811] = 206.48$, $P < .001$; HC < PC = PP < IED = IED/PP by Tukey HSD; Composite Impulsivity ($F[4, 770] = 74.37$, $P < .001$; HC < PC = PP < IED < IED/PP by Tukey HSD). Similar results were found for socially deviant trait scores (Composite Aggression: $F[4, 1{,}048] = 352.05$, $P < .001$, HC < PC < PP < IED < IED/PP by Tukey HSD; Composite Anger: $F[4, 811] = 220.30$, $P < .001$; HC < PC < PP < IED < IED/PP by Tukey HSD; Composite Impulsivity ($F[4, 770] = 84.54$, $P < .001$; HC < PC < PP = IED < IED/PP by Tukey HSD). Adding the demographic variables to the statistical models did not change these results.

PCL-SV correlates: aggression, anger, and impulsivity. In these analyses, we explored the dimensional relationships between PCL-SV scores and the composite behavioral dimensions. Across all participants, significant zero-order correlations were observed between PCL-SV Total scores and each of the composite behavioral variables Composite Aggression ($r = .58$, $P < .001$), Anger ($r = .52$, $P < .001$), and Impulsivity ($r = .52$, $P < .001$) scores. Partial correlational analysis, controlling for the other two composite variables, revealed lower correlations for each composite variable with only aggression and impulsivity exceeding statistical significance (Aggression: partial $r = .33$, $P < .001$; Anger: partial $r = .06$, $P < .116$; Impulsivity: partial $r = .25$, $P < .001$). Partial correlations differed as a function of PCL-SV sub-scores where correlations with socially deviant trait scores were significantly greater than those with callous/unemotional trait scores (Aggression: $r = .32$ vs. $r = .24$, $t_{730} = 2.48$, $P < .001$; Anger: $r = .11$ vs. $r = -.01$, $t_{730} = 3.55$, $P = .013$; Impulsivity: $r = .28$ vs. $r = .15$, $t_{730} = 3.97$, $P < .001$).

PCL-SV correlates: global psychosocial function. In addition to relationships with aggression, anger, and impulsivity, PCL-SV defined groups displayed an inverse relationship with GAF score. ANOVA of GAF scores ($F[4, 1{,}047] = 430.10$, $P < .001$) revealed that PP (55.5 ± 10.0) and IED (55.7 ± 7.8) participants had similar GAF scores that were significantly lower than those among HC (84.0 ± 5.5) and PC (66.2 ± 12.1) participants, and significantly higher than those among IED/PP participants (50.7 ± 8.5). In addition, PCL-SV scores were significantly, and inversely, correlated with GAF scores across participants (Total: $r = -.63$, $P < .001$; callous/unemotional trait scores: $r = -.44$, $P < .001$; Part 2: $r = -.66$, $P < .001$), with the correlation between GAF and socially deviant trait scores being significantly greater than that with callous/unemotional trait scores ($t_{1050} = 8.68$, $P < .001$). Multiple regression correlation analysis confirmed a much larger relationship for socially deviant traits, compared with callous/

unemotional traits with GAF scores (callous/unemotional traits: $B = -0.529 \pm 0.168$, $\beta = -.089$, $P = .002$ vs. socially deviant traits: $B = -2.753 \pm 0.129$, $\beta = -.607$, $P < .001$).

PCL-SV score as a function of primary diagnostic group. Finally, we explored the relationship of PCL-SV scores as a function of primary diagnostic group (i.e., HC, PC, IED). As expected, ANOVA of PCL-SV Total scores revealed significant group differences ($F[2, 1{,}050] = 261.47$, $P < .001$) with IED participants having the highest PCL-SV Total score, followed by PC, then HC, participants (IED: 8.01 ± 4.17 vs. 4.08 ± 4.17 vs. 0.64 ± 4.16; all comparisons $P < .05$ by Tukey HSD). Follow-up MANOVA analysis, using the PCL-SV sub-scores as dependent variables, revealed similar differences by primary diagnostic group (Wilks $\lambda = .63$; $F[4, 2{,}098] = 137.86$, $P < .001$) for callous/unemotional traits ($F[2, 1{,}050] = 98.08$, $P < .001$; HC < PC < IED; $P < .05$ by Tukey HSD) and socially deviant trait ($F[2, 1{,}050] = 305.74$, $P < .001$; HC < PC < IED; $P < .05$ by Tukey HSD). Repeated measures MANOVA revealed that socially deviant trait scores were significantly greater than callous/unemotional trait scores as a function of group (Wilks $\lambda = .89$, $F[1, 1{,}050] = 132.94$, $P < .001$) and as a function of the interaction of group × PCL-SV sub-score (Wilks $\lambda = .86$, $F[2, 1{,}050] = 83.27$, $P < .001$). For the interaction, PC and IED participants differed significantly as a function of type of PCL sub-score (PC/callous/unemotional traits: 1.73 ± 2.29 vs. PC/socially deviant traits: 2.35 ± 2.59, $P < .05$ by Tukey HSD) and IED (IED/callous/unemotional traits: 2.87 ± 2.30 vs. IED/socially deviant traits: 5.14 ± 2.59; $P < .05$ by Tukey HSD); HC participants did not differ by PCL-SV sub-score.

Logistic regression analysis with IED status (Yes/No) as the dependent variable, and the two PCL-SV sub-scores as covariates, confirmed that socially deviant [$B \pm \text{SE} = 0.46 \pm 0.04$, Wald = 176.17, df = 1, Exp(B) = 1.59 (95% CI: 1.48–1.70), $P < .001$], rather than callous/unemotional [$B \pm \text{SE} = 0.02 \pm 0.04$, Wald = 0.04, df = 1, Exp(B) = 1.02 (95% CI: 0.95–1.10), $P = .546$], traits were associated with differences in PCL-SV sub-scores in IED status. Adding composite scores for aggression, anger, and impulsivity, as additional covariates, marginally reduced the magnitude, but not the statistical significance, of the relationship between social deviant traits and IED Status [$B \pm \text{SE} = 0.32 \pm .06$, Wald = 31.12, df = 1, Exp(B) = 1.37 (95% CI: 1.23–1.53), $P < .001$]. In addition, both aggression [$B \pm \text{SE} = .1.67 \pm .23$, Wald = 51.40, df = 1, Exp(B) = 5.32 (95% CI: 3.37–8.39), $P < .001$] and anger [$B \pm \text{SE} = 0.97 \pm .18$, Wald = 27.60, df = 1, Exp(B) = 2.63 (95% CI: 1.83–3.77), $P < .001$], but not impulsivity [$B \pm \text{SE} = -0.15 \pm .17$, Wald = 0.72, df = 1, Exp(B) = 0.86 (95% CI: .62–1.21, $P = .397$], scores were significantly related to IED status. Inspection of the Exp(B) values revealed that Exp(B) values were nearly fourfold higher for aggression, and nearly twofold higher for anger, compared with social deviant traits. Thus, in the final model, aggression, anger, and socially deviant psychopathic traits (but not impulsivity or callous/unemotional psychopathic traits) appeared to relate to the presence or absence of IED.

Study II: Relationships Between PCL-SV Status and Scores and Familial IED, 5-HT Biomarkers, and Treatment Outcome With Anti-Aggressive Modalities

Participants. Study II constituted a reanalysis of five published studies to investigate the nature of the relationship, if any, between psychopathy and familial, biological marker, and treatment response variables relevant to IED (Coccaro, 2010; Coccaro et al., 2009, 2010a, 2010b; McCloskey et al., 2008). The first was a family history study of IED in first-degree relatives of probands with IED and without IED (Coccaro, 2010); these participants had the following demographic characteristics: mean age: 35.9 ± 9.7 years; sex: 65.8% men; ethnicity: 56.2% while, 41.1% African-American, 2.8% Other; mean Hollingshead SES score: 28.1 ± 10.3. The second was a pharmaco-challenge study with the 5-HT releasing agent D-fenfluramine in healthy controls and in participants with personality disorder (Coccaro et al., 2010a); mean age: 32.8 ± 9.6 years; sex: 68.7% men; ethnicity: 72.0% White, 24.7% African-American, 3.3% Other; mean Hollingshead SES score: 30.9 ± 10.0. The third was a study of the number of platelet 5-HT transporter binding sites in participants with personality disorder (Coccaro et al., 2010b); mean age: 34.5 ± 9.1 years; sex: 83.0% men; ethnicity: 61.0% White, 37.0% African-American, 2.0% other; mean Hollingshead SES score: 28.8 ± 10.0. The fourth was a randomized clinical trial of fluoxetine versus placebo in IED subjects (Coccaro et al., 2007); mean age: 37.0 ± 8.9 years; sex: 77.0% men; ethnicity: 64.1% White, 30.5% African-American, 5.41% Other; mean Hollingshead SES score: 33.7 ± 11.5. The last was a controlled, randomized clinical trial of cognitive behavioral therapy versus wait-list in IED subjects (McCloskey et al., 2008); mean age: 37.4 ± 7.3 years; sex: 66.7% men; ethnicity: 68.7% White, 22.2% African-American, 8.8% Other; mean Hollingshead SES score: 42.8 ± 11.6. Further details on the participants and methods involved in these studies can be found in the source publications.

RESULTS

The results of these re-analyses are summarized in Table II. The presence of "possible" and "highly likely" psychopathic personality was, respectively, 12.6% and 5.3% (Mean PCL-SV score = 7.7 ± 5.0) among

TABLE II. Effect of PCL-SV Psychopathy on IED in Published Studies

	Family History Study of IED (Coccaro, 2010)	5-HT Pharmaco-Challenge Study (Coccaro et al., 2010a)	Platelet 5-HT Transporter Study (Coccaro et al., 2010b)	Fluoxetine Treatment Study in IED (Coccaro et al., 2009)	Cognitive Behavioral Treatment Study in IED (McCloskey et al., 2008)
Subjects	32 IED 32 controls	100 Personality disorder (54 IED) 50 controls	100 Personality disorder (44 IED)	100 IED (65 active Rx)	45 IED (30 active Rx)
Psychopathic personality (%)	3%	8%	8%	7%	16%
Mean (+SD) PCL-SV total score	CON: 2.0 ± 2.7	CON: 0.5 ± 1.1	IED: 6.2 ± 3.8	IED: 5.1 ± 2.7	IED: 5.5 ± 2.9
	IED: 5.3 ± 2.9 PP: 14.0 ± 0.0	IED: 5.4 ± 3.1 PP: 16.4 ± 2.9	PP: 16.9 ± 2.7	PP: 15.4 ± 2.1	PP: 16.5 ± 2.3
Primary study finding	Morbid risk of IED in relatives: IED > controls	PRL[d-FEN] response: IED < HC	Bmax ^{3}H-Paroxetine: IED < NON-IED	Reduction in OAS-M aggression scores: fluoxetine > placebo	Reduction in OAS-M aggression scores: CBT > wait-list
Effect of psychopathic personality	Number of PP subjects too small to compare	PRL[d-FEN] Response: IED < HC (P < .001) PP = HC	Bmax ^{3}H-Paroxetine: IED = PP	OAS-M aggression score at endpoint: effect of PP: F[1,95] = 0.28 (P = .60)	OAS-M aggression score at endpoint: effect of PP: F[1,40] = 1.43 (P = .24)

the 190 IED participants involved in these studies. Since the presence of PCL-SV defined psychopathy was not exclusionary for study entry, the proportion of IED participants with "highly likely" PCL-SV psychopathy (5.3%) examined in these studies was relatively low, though not as low as that in the general population which has been estimated at 1.2% in a sizable community sample (Neumann & Hare, 2008). The presence of psychopathic personality did not change the primary finding of the studies regarding IED, and PCL-SV scores did not correlate significantly with the primary outcome measures in the two biomarker studies (e.g., prolactin response to D-fenfluramine challenge and PCL-SV Total score: $r = .00$, $P > .95$; callous/unemotional trait score: $r = .08$, $P > .45$; socially deviant trait score: $r = -.08$, $P > .45$; Bmax for 3-H-Paroxetene Binding and PCL-SV Total: $r = -.09$, $P = .40$, callous/unemotional trait score: $r = -.12$, $P = .25$, socially deviant trait score: $r = -.03$, $P = .81$).

DISCUSSION

This is the first study to examine the relationship between DSM-5 IED and psychopathic personality. The impetus to explore this relationship comes from the fact that antisocial personality disorder, a personality disorder related, but not identical, to psychopathic personality, was a relative exclusion for DSM-IV IED and that aggression, in general, is an important feature of psychopathic personality.

The results of Study I demonstrate that PCL-SV psychopathic personality, as defined in this study, is significantly more frequent among DSM-5 IED subjects than in healthy and psychiatric participants. While not a population-based study, a rate of 5.9% for "highly likely" psychopathic personality in the DSM-5 IED group is most likely greater than the reported rate of 1.2% of the same in community studies (Neumann & Hare, 2008). Moreover, given the relationship with aggressive behavior among psychopaths an elevated rate of psychopathy among IED subjects was expected. That said, the rate of psychopathy in these IED subjects was far from a rate that could suggest that one is explained by the other (even if one includes "possible" psychopaths in the analysis). In addition, it is noteworthy that mean PCL-SV total and subtype scores for all IED subjects were in the non-psychopathic range.

Among the two subtypes of psychopathic personality examined, rates, and scores of the socially deviant subtype were higher and greater than those for the callous/unemotional subtype. Given the inclusion of aggressive-related behaviors in socially deviant subtype, this was expected. More importantly, when both subtypes were examined in the same multiple regression model, the β coefficient for the socially deviant psychopathy

were more than 10 times that for callous/unemotional psychopathy which only reached a trend. When the core composite behavioral variables were added to the model, β coefficients for socially deviant psychopathy was reduced by half while those for aggression and anger were as high or higher. This suggests that the relationship between DSM-5 IED and psychopathy may act through socially deviant, rather than callous/unemotional, psychopathy as well as through aggression and anger to nearly equal degrees.

Comparing trait aggression, anger, and impulsivity scores as a function of the PCL-SV group revealed that IED participants without psychopathic personality have substantially greater trait aggression and trait anger than PC participants with psychopathic personality. This suggests that psychopathy, alone, cannot explain the heightened aggression and anger of IED participants, though it can help explain the greater trait aggression scores of IED-PP participants. The high trait impulsivity scores in IED-PP participants, in contrast, may be explained by the simple addition of impulsivity, which was equal in PP and in IED participants.

The results from the re-analyses performed in Study II showed that the vast majority of subjects in studies providing evidence for the DSM-5 diagnosis of IED (Coccaro, 2012) were not psychopathic. The percentage of IED participants with "possible" or "highly likely" psychopathic personality ranged from only 3% to 16% across the studies, and the highest mean PCL-SV Total score for participants in these studies was well below the lower limit for "possible psychopathy" (i.e., $\geq$13). Where participants with psychopathic personality could be compared with non-psychopathic individuals, the data suggest that the presence of psychopathic personality had limited, if any, impact on the outcome variables studied. Finally, no meaningful correlations between PCL-SV scores and the two biomarkers that were previously studied were found. This is in contrast to the significant inverse relationships observed previously with the two biomarkers and measures of aggression (e.g., Coccaro et al., 2010a,b).

These two studies have both strengths and limitations. The sample size for Study I is large and contains participants that were assessed comprehensively with validated measures of aggression, anger, impulsivity, and psychopathy. While the sample sizes for the five groups were generally large, the number of participants with "psychopathy only" was small and it is possible that a larger group would have been associated with different results. Other limitations include the fact that the participants, while recruited from the community, were not studied as part of a population-based cohort and were not selected from a clinical population. Regarding this latter point, 73% of the psychiatric (PC, IED) participants reported a formal history of psychiatric treatment and/or a history of one or more episodes of a behavioral disturbance during which the participant (or others) thought they should have sought psychiatric evaluation and/or treatment (but did not). Accordingly, most of the participants in this report may be similar to individuals who would have been recruited from a clinical setting. In addition, this study is cross-sectional and therefore preclude making causal inferences. For Study II, the small numbers of participants meeting criteria for PCL-SV psychopathic personality limits the power of this analysis to detect small potential differences due to psychopathy. However, there is sufficient extant data in individuals who were, or were likely to have been, psychopaths to support the findings we report. For example, positive treatment responses to anti-aggressive agents have been shown in prison inmates with reactive (i.e., "impulsive"), but not proactive (i.e., "premeditated") aggression and/or psychopathic behavior (Barratt et al., 1997; Sheard et al., 1976).

In conclusion, this study finds that only a modest proportion of IED participants display clinically substantial features of psychopathy and that measures of trait aggression and anger, rather than those of psychopathy, are the strongest correlates of IED. Where features of psychopathy are present in those with IED, it occurs through the socially deviant, rather than the callous/unemotional set of psychopathic traits. Reanalysis of previously reported findings in IED subjects finds little evidence for any impact of the presence of psychopathy on these findings compared with various control subjects. That said, it will be desirable to indicate the presence of psychopathic personality, where possible, in future studies of human aggression.

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