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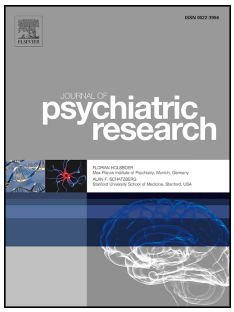

History of childhood maltreatment in intermittent explosive disorder and suicidal behavior

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HISTORY OF CHILDHOOD MALTREATMENT IN INTERMITTENT EXPLOSIVE DISORDER AND SUICIDAL BEHAVIOR

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ABSTRACT

Intermittent Explosive Disorder (IED) is a relatively common disorder of impulsive aggression that typically emerges by adulthood. Maltreatment in childhood (CM) may contribute to the development of IED, but little is known about the association between CM and IED, including about how subtypes of CM may specifically relate to IED. This study aimed to test the association between CM and IED diagnosis. A second aim was to examine history of CM in suicide attempters, and to explore whether impulsivity and aggression account for the relationship between CM and suicide attempt (SA). Adults with Intermittent Explosive Disorder (IED; n=264), with non-IED psychiatric (Axis I or II) disorders (psychiatric controls; PC; n=199), and with no psychiatric disorder (healthy control subjects; HC; n=185) were assessed for history of childhood maltreatment, aggression, impulsivity, and history of SA. IED subjects reported significantly greater CM compared to PC and HC subjects, and suicide attempters (n=62) reported greater CM compared to non-attempters (n=586). Physical abuse in childhood was independently associated with IED, while sexual abuse and emotional abuse were independently associated with SA. Impulsivity and aggression were potential mediators of the relationship between physical abuse and IED and emotional abuse and SA, but sexual abuse was associated with SA independently of aggression and impulsivity. The results suggest pathways by which environmental factors may influence impulsivity and aggression and, in turn, clinically significant self- and other-directed aggression.

1. INTRODUCTION

Aggression and suicide are destructive behaviors that exact a considerable toll on individuals, families, and society. Each year, approximately 1.6 million people die as a result of violence, both self- and other-directed (WHO, 2009), and these events and other non-lethal forms of aggression (i.e., interpersonal assaults and suicide attempts) have substantial economic costs (Czernin et al., 2012; WHO, 2004). Despite the severity of these behaviors they are relatively common. In the National Comorbidity Study (NCS), 4.6% of respondents reported making a suicide attempt in their lifetime (Kessler, Borges, & Walters, 1999), while the lifetime prevalence of clinically significant aggression, as defined by Intermittent Explosive Disorder (IED) DSM-IV criteria, was reported as high as 7.3% (Kessler et al., 2006).

Impulsive aggression is the core feature of IED and is also a risk factor for suicidal behavior, making it an important target of efforts to reduce both self- and other-directed aggressive behavior. Behavioral genetics studies indicate that both genetic and environmental factors contribute to the development of aggression (Coccaro, Bergeman, Kavoussi, & Seroczynski, 1997; Miles & Carey, 1997; Yeh, Coccaro, & Jacobson, 2010); however, relatively little is known about environmental variables which may contribute to the development of clinically significant impulsive aggression (IED). Understanding the factors that promote the development of impulsivity and aggression (and which may in turn increase the likelihood of suicide attempt and persistent aggression) is thus an important scientific and therapeutic goal.

One set of environmental circumstances that has been shown to contribute to the development of impulsive aggression is childhood maltreatment (CM). CM includes

experiences of physical, emotional, and sexual abuse, and emotional and physical neglect. CM predicts a range of negative outcomes, including psychopathology (Briere & Elliott, 2003; Green et al., 2010; Lobbestael, Arntz, & Bernstein, 2010; Scott, McLaughlin, Smith, & Ellis, 2012), aggression (Singer, Miller, Guo, Flannery, & Frierson, 1999; Song, Singer, & Anglin, 1998), and suicidal behaviors (Miller, Esposito-Smythers, Weismoore, & Renshaw, 2013; Silverman, Reinherz, & Giaconia, 1996), but little is known specifically about the role of CM in the development of IED. Individuals with IED have been found to have significant histories of trauma (e.g., accidents, disaster-related traumas; Fincham, 2011), and interpersonal traumas and traumas experienced early in life are particularly predictive of IED (Nickerson, Aderka, Bryant, & Hofmann, 2012), suggesting that CM may significantly increase the risk of developing IED. Furthermore, childhood adversities related to a maladaptive family environment have been shown to be particularly predictive of later psychopathology in general (Green et al., 2010; McLaughlin et al., 2012). Studies on the effects of CM on suicidality suggest that most forms of CM increase the risk of suicide attempt when considered separately (Miller et al., 2013), but that sexual, physical, and emotional abuse are particularly robust predictors when different forms of CM are considered together in multivariate analyses (Beautrais, Joyce, & Mulder, 1996; Hacker, Suglia, Fried, Rappaport, & Cabral, 2006; Joiner et al., 2007; Ystgaard, Hestetun, Loeb, & Mehlum, 2004).

In addition to being a core feature of IED, impulsive aggression is also associated with Antisocial Personality Disorder (ASPD) and Borderline Personality Disorder (BPD). Further, suicide attempters and completers have been found to have higher levels of impulsivity and aggression (Brodsky et al., 2001; Dumais et al., 2005;

Mann, Waternaux, Haas, & Malone, 1999). Brodsky (2001) examined childhood abuse history, BPD, and impulsive and aggressive personality traits as predictors of lifetime suicide attempt. Participants reporting a history of childhood abuse were more likely to have attempted suicide, had higher reported levels of impulsivity and aggression, and were more likely to meet criteria for BPD. However, when considered together, childhood abuse, but not BPD, impulsivity, or aggression, contributed uniquely to the prediction of SA.

The purpose of this study was to examine the associations between early experiences of abuse and neglect and clinically significant aggressive and self-aggressive behavior in an adult sample of research volunteers with and without psychopathology. We first sought to extend prior research on the association between trauma and IED by using a well-validated measure of childhood maltreatment that distinguishes different forms of CM including physical and sexual abuse and neglect. Specifically, we compared participants with IED to non-IED psychiatric control subjects (PC) and healthy control (HC) subjects on subtypes of CM and total CM. Next, we examined which forms of childhood maltreatment were independently associated with impulsive and aggressive traits, and with a lifetime diagnosis of IED. Finally, we explored impulsivity and aggression as potential mediators of the relationship between CM and IED. We conducted similar analyses for lifetime history of suicide attempt. This was done to replicate and extend prior findings by examining potential specific associations between type of childhood abuse and suicide attempt as well as the roles of impulsivity and aggression in these relationships. These relationships were tested in a series of hierarchical models. In order test whether these effects were independent of

Antisocial and Borderline Personality Disorders, as these are associated with impulsive aggression, suicide risk, and early life trauma (Beautrais et al., 1996; Brodsky et al., 2001; Lobbestael et al., 2010; Silverman et al., 1996), we included these diagnoses as covariates in a final logistic regression model. We predicted that: 1) IED subjects would report more childhood maltreatment compared with healthy control and psychiatric control subjects; 2) subjects with history of suicide attempt would report more CM and have higher scores on aggression and impulsivity; and 3) trait aggression and impulsivity (assessed dimensionally) would at least partially explain the relationship between CM and later IED and SA, suggesting that CM may increase impulsivity and aggressiveness and thereby increase the risk of negative outcomes.

2.0 METHODS

2.1 Subjects. Six-hundred-forty-eight medically healthy subjects participated in this study as research volunteers. All subjects were systematically evaluated with regard to aggression, impulsivity, and other behaviors as part of a larger program designed to study correlates of impulsive aggression and other personality-related behaviors in human subjects. Subjects were recruited from public service announcements and through media advertisements seeking individuals who: a) were experiencing psychosocial difficulty related to one or more Axis I and Axis II conditions or, b) had no evidence of psychopathology. All subjects provided written informed consent as approved by the Committee for the Protection of Human Subjects (IRB). By study exclusion criteria, no subject had current alcohol or other drug dependence and none had a life history of mania/hypomania, schizophrenia, or delusional disorder.

2.2 Diagnostic Assessment. Axis I and Axis II personality disorder diagnoses were made according to DSM-IV criteria (Amercian Psychiatric Association, 1994). Diagnoses of Intermittent Explosive Disorder (IED) were made by research criteria (Coccaro, 2011) and all IED subjects 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; First et al., 1997) for Axis I disorders and the Structured Interview for the Diagnosis of DSM Personality Disorder (Pfohl et al., 1997) for Axis II disorders; (b) clinical interview by a diagnostic rater with at least master's level training; and; and (c) a review of all other available clinical data. 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 rater was deemed reliable with the trainer. This process resulted in good to excellent inter-rater reliabilities (mean kappa of .84 $\pm$ .05; range: .79 to .93) across mood, anxiety, substance use, impulse control, and personality disorders. Final diagnoses were assigned by team best-estimate consensus procedures (Klein et al., 1994; Leckman et al., 1982) involving research psychiatrists and clinical psychologists as previously described (Coccaro et al., 2011). This methodology has previously been shown to enhance the accuracy of diagnosis over direct interview alone (Kosten & Rounsaville 1992).

IED participants were those with a lifetime diagnosis of IED. Psychiatric control participants had a current or lifetime syndromal (Axis I) or personality (Axis II) disorder. By definition, none of the 185 healthy control subjects had a current or lifetime history of

any syndromal or personality disorder. Demographic characteristics of the subjects are displayed in Table 1. Rates of syndromal and personality disorders among the 199 PC and 264 IED subjects are displayed in Table 2. In addition to meeting criteria for syndromal and personality disorders, a majority of PC and IED subjects (71%) reported a history of psychiatric treatment (57%) or of a behavioral disturbance for which the subject, or others, thought they should have sought mental health services but did not (46%). History of suicide attempt was assessed during the diagnostic interview and underwent the same best estimate procedure. An act was considered a suicide attempt if it involved engaging in a behavior with the conscious (even if ambivalent) intent to die by means the subject believed could end his or her life.

2.3 History of Childhood Maltreatment. History of CM was assessed using the 28-item Childhood Trauma Questionnaire (CTQ; Bernstein et al., 1994). Five subscales of the CTQ assess different aspects of CM including physical abuse, emotional abuse, sexual abuse, physical neglect, and emotional neglect and the scale has been shown to have good psychometric properties (Roy & Perry 2004). The scale also yields a total child maltreatment score. Cronbach's alphas were adequate to excellent for all CTQ subscales (alphas > .76; see Table 3).

2.4 Aggression, Impulsivity, and Suicide Attempt. Aggression was assessed by the Aggression subscale from the Life History of Aggression (LHA; Coccaro et al., 1997). LHA-Aggression (LHA-A) assesses the number of aggressive acts a person has engaged in over the lifespan, including number times a person has gotten into physical fights, assaulted someone, and purposely damaged property. Impulsivity was assessed

using the Barratt Impulsivity Scale 11th Edition (BIS-11; Patton et al., 1995). The BIS-11 assesses the tendency to act impulsively as a personality trait and includes separate scales for motor, attentional, and non-planning impulsivity. The BIS-11 total score was used in this study. Cronbach's alphas for the LHA-A and BIS-11 showed excellent reliability (see Table 3).

2.5 Statistical Analysis. Relationships among categorical variables were analyzed using Fisher's Exact Test (FET). Between groups differences on dimensional measures were assessed using analysis of variance (ANOVA) and t-tests. Levene's test was used to assess homogeneity of variance. Where significant heterogeneity was present, Brown-Forsyth statistic (F*) or t-test for unequal variances was used. Post-hoc testing was carried out using Tukey's HSD or Games-Howell test as appropriate. Correlational analyses were conducted using Pearson's correlation. Multivariate associations between continuous variables were examined using multiple linear regression. The effects of predictor variables on IED diagnosis and suicide attempt were assessed using hierarchical logistic regression. Statistical significance of the parameter estimate (β) for each predictor was evaluated using Wald χ^2 statistic. Odds ratios (ORs) with 95% confidence intervals are adjusted for covariates in the model. For ease of interpretation, scale scores (i.e., childhood trauma, aggression, and impulsivity) were z-transformed prior to entry into the model. Thus, ORs for these variables represent the change in odds associated with a 1 standard deviation (SD) change in the predictor variable. A two-tailed alpha of 0.05 was used to denote statistical significance for all analyses.

3.0 RESULTS

3.1 Demographic and Psychiatric Comorbidity Characteristics of the Sample (Tables 1 and 2). Participants ranged in age from 18 to 70 (M=34.0, SD=9.8). The self-identified racial composition of the sample was 57% white, 33% African American, 4% Asian American, 4% Hispanic, and 2% other. The HC, PC, and IED groups differed in age (IED > PC > HC) but not gender or racial composition or Hollingshead SES scores. Suicide attempters were older than non-attempters and were more likely to be female (see Table 1), but did not differ in racial composition or SES. Psychiatric diagnoses in the IED and PC groups and the SA- and SA+ groups are shown in Table 2. All SA+ participants had a lifetime history of Axis I disorder compared to 61.6% of participants with no lifetime suicide attempt (SA-; $p<.001$). 96.8% of SA+ group had an Axis II personality disorder, compared to 55.6% of the SA- group ($p<.001$).

3.2 Bivariate and multivariate relationships between childhood trauma, impulsivity and aggression. Bivariate correlations between subscales of the Childhood Trauma Questionnaire and the LHA-A and BIS-11 are shown in Table 3. All correlations were highly significant (all $ps<.001$). Bivariate correlations between trauma subscales ranged from moderate (e.g., Sexual Abuse-Emotional Neglect, $r=.31$) to large (e.g., Emotional Neglect-Emotional Abuse, $r=.71$) in size. The correlation between aggression and impulsivity was moderate-to-large ($r=.44$), and the correlations between CM subscales and aggression and impulsivity were moderate in size ($rs=.18$-$.37$). The standardized CM subscales were entered into separate multivariate analyses predicting aggression and impulsivity. CM explained 16% of the variance in aggression, $F(5, 642)=25.20$,

p<.001. Physical abuse (β=1.52, t=4.20, p<.001) and emotional abuse (β=0.99, t=2.36, p=.018) were significant independent predictors of life history of aggression. CM explained 14% of the variance in impulsivity, F(5, 642)=20.48, p<.001. Emotional abuse (β=2.57, t=3.75, p<.001) was the only independent predictor of impulsivity.

3.3 Psychiatric Group and CTQ scores. One-way ANOVA revealed a significant difference in Total CTQ scores as a function of subject group (F*[2,586] = 72.39, p < .001). Post-hoc testing demonstrated that Total CTQ scores were highest among IED subjects (M=52.2, SD=18.2) and were significantly higher than those of PC subjects (M=44.8, SD=16.0, d=.43) and HC subjects (M=35.2, SD=9.5; d=1.11; Figure 1, left). PC subjects reported more CM than HC subjects (d=0.72). IED participants also had significantly higher trauma scores on four of five subscales of the CTQ compared to both the PC and HC participants (see Table 4). IED participants had marginally higher scores on reported sexual abuse (p=.082) compared to PC participants, and significantly higher scores compared to HC participants (p<.001). The five CTQ subscale scores were entered into a logistic regression with IED status as the outcome and age, race (white vs. non-white), gender, and SES score entered in a first step as covariates. The addition of the trauma scales significantly improved the fit of the model (Table 5A, Model 1). Physical abuse was the only trauma scale independently associated with IED. Emotional abuse was predictive of IED status at the level of a trend (p = .096). No other CTQ subscale scores were independently predictive of IED.

3.4 Hierarchical models of childhood trauma, impulsive aggression, and IED. To test whether aggressive and impulsive traits account for the relationship between childhood maltreatment and IED diagnosis, aggression (LHA-A scores) and impulsivity (BIS-11 scores) were entered into the logistic regression model from Section 3.3 in a third step. Changes in predictors from significant to non-significant would suggest that aggression or impulsivity accounted for the relationship between trauma and later IED. The addition of aggression and impulsivity in Step 3 significantly improved model fit (Table 5A, Model 2). After this step, no trauma variables remained significant predictors of IED status (all ps > .57). Specifically, the relationship between physical abuse and IED became non-significant. Emotional abuse was no longer significant at the level of a trend. The LHA-A and BIS-11 both significantly predicted whether someone met criteria for IED during the lifetime.

To assess whether childhood trauma predicts IED independently of the effects of Antisocial and Borderline Personality Disorders, a final logistic regression model was analyzed with ASPD and BPD entered in a separate step after the trauma variables. After entering these variables in Step 3, Physical Abuse continued to be a significant predictor of IED (Figure 5A, Model 3). ASPD and BPD were also significant predictors of IED. When aggression and impulsivity were added in a final step, aggression continued to significantly predict IED status even given ASPD and BPD in the model, but impulsivity was associated with IED only at the level of a trend (p=.057; see Table 5A, Model 4 for the final model).

3.5 Suicide Attempt History and CTQ scores. Sixty-two participants in the full sample (9.6%) reported a past suicide attempt. Participants with a past suicide attempt reported higher Total CTQ scores (M=61.9, SD=20.9) compared to those with no history of suicide attempt (M=43.3, SD=15.5; t[646]= -6.83, p<.001]; Figure 1, right, d=1.16). Suicide attempters also had greater lifetime self-reported aggression (d=.84) and impulsivity (d=.93; Table 4). Hierarchical logistic regression analysis with SA history as the dependent variable and age, gender, race, and SES entered as covariates in the first step, and the five CTQ subscales entered as predictors in the second step, again showed that including childhood trauma in the model significantly improved the fit (Table 5B, Model 1). CTQ Emotional Abuse and CTQ Sexual Abuse were independent predictors of lifetime suicide attempt. No other CTQ subscale scores independently predicted history of suicide attempt.

3.6 Hierarchical models of childhood maltreatment, impulsive aggression, and suicide attempt. To test whether aggressive and impulsive traits account for the relationship between childhood trauma and suicide attempt, aggression and impulsivity scores were entered into the logistic regression model from Section 3.4 in a third step. As was the case for IED, adding aggression and impulsivity significantly improved model fit (Table 5B, Model 2). After this step, Emotional Abuse was no longer a significant predictor of suicide attempt (p=.158). However, sexual abuse continued to significantly predict suicide attempt even with the addition of aggression and impulsivity to the model. Aggression and impulsivity were also significant predictors of suicide attempt.

To assess whether childhood maltreatment predicts suicide attempt even when accounting for Antisocial and Borderline Personality Disorders, the same logistic regression model was run but with ASPD and BPD entered in a separate step after the trauma variables and before the aggression and impulsivity variables. When entered into the model, ASPD and BPD were significant predictors of suicide attempt (Figure 5B, Model 3). Emotional Abuse (previously a significant predictor of suicide attempt) was no longer significant (p=.105). Sexual Abuse continued to predict suicide attempt over and above the effects of ASPD and BPD. When aggression and impulsivity were added to the model in a final step (Figure 5B, Model 4), the effect of aggression on suicide attempt was not significant (p=.108) while impulsivity continued to significantly predict suicide attempt (p=.008).

4.0 DISCUSSION

In this study, we examined the role of childhood maltreatment (CM) as a predictor of self- and other-directed aggression, namely, lifetime suicide attempt and Intermittent Explosive Disorder diagnosis (IED). We also examined the roles of aggression and impulsivity as potential mediators of these relationships. As expected, individuals diagnosed with IED reported significant histories of CM. IED participants reported more extensive abuse and neglect histories for every type of CM compared to both healthy individuals and individuals with non-IED psychiatric disorders. This is the first study of which we are aware to examine specific relationships between types of childhood maltreatment and IED, and is consistent with other research pointing to high rates of past traumatic exposure in individuals with IED (Fincham, 2011; Nickerson et

al., 2012). When all forms of CM were considered together and demographic variables were accounted for, only physical abuse specifically predicted IED diagnosis, while other forms of abuse and neglect did not. Previous research has shown that early traumatic life events and CM are associated with the development of a range of psychopathology, including disruptive behavior disorders (McLaughlin et al., 2012) and aggression (Briere & Runtz, 1990; Dodge, Bates, & Peitit, 1990). Other research suggests that physical abuse in childhood may be a specific risk factor for the development of ASPD (Cohen et al., 2013; Lobbestael et al., 2010); however, with respect to the latter, we found that, even after including ASPD and BPD in the logistic regression model, physical abuse continued to predict diagnosis of IED. Therefore, exposure to physical abuse in childhood may confer risk for clinically significant aggression over and above the effects of ASPD. This finding accords with research demonstrating the distinctiveness of IED from ASPD and BPD, particularly with regard to the presence of aggression (Coccaro, 2012). Other studies have failed to find a relationship between sexual abuse and violent behavior when other traumatic exposures (including exposure to physical violence) are considered simultaneously (Song et al., 1998).

We also used the hierarchical logistic regression model to test whether the relationship between CM and IED is accounted for by aggression, impulsivity, or both. CM accounted for approximately 15% of the variance in aggression and impulsivity. Physical aggression and emotional abuse independently predicted aggression and emotional abuse independently predicted impulsivity when all forms of CM were considered simultaneously. When aggression and impulsivity were entered into the

model after CM subscales, the relationship between physical abuse and IED became non-significant, and both aggression and impulsivity showed strong independent relationships to the disorder. This finding suggests that the experience of physical abuse in childhood may increase the propensity to engage in aggressive and impulsive behaviors and in turn increase the likelihood of being diagnosed with IED. History of aggression also strongly predicted IED diagnosis over and above ASPD and BPD. The addition of aggression and impulsivity to the model rendered the relationship between IED and BPD nonsignificant, and in the full model (Table 5A Model 3) the relationship between impulsivity and IED was reduced to a trend, suggesting that impulsivity is a risk factor for IED that is largely shared with BPD. In contrast, ASPD continued to predict IED even with aggression and impulsivity accounted for in the model.

In addition to examining the relationship between CM and IED, we also examined the relationship between CM and suicide attempt. Suicide attempters reported greater levels of CM overall and greater self-reports of each subtype of CM. Suicide attempters also had greater life histories of aggression and reported more impulsivity, consistent with prior research (Brodsky et al., 2001; Mann et al., 1999). When subtypes of CM were considered together and demographic variables were accounted for, both emotional abuse and sexual abuse independently predicted SA. This accords with previous research showing that sexual abuse and/or emotional abuse are significant and independent predictors of SA (Beautrais et al., 1996; Hacker et al., 2006), even when other adverse environmental conditions are considered. In contrast to some prior studies, we did not find a specific relationship between physical abuse and suicidal behavior (Joiner et al., 2007; Ystgaard et al., 2004).

Adding aggression and impulsivity to the model made non-significant the relationship between emotional abuse and SA, suggesting that these may mediate the relationship between emotional abuse and SA. Indeed, an emotionally abusive home environment is thought to contribute to emotional and behavioral dysregulation that are associated with suicidal behavior (Linehan, 1993). Sexual abuse continued to significantly predict SA even after including aggression and impulsivity in the model, suggesting that it is associated with suicide attempt via other pathways than aggression and impulsivity. Accordingly, in multiple regression analyses, sexual abuse did not independently predict impulsivity or aggression. Sexual abuse also continued to predict SA even after accounting for ASPD and BPD. When considering all variables in the final model, female gender, sexual abuse, BPD diagnosis, and impulsivity each made unique contributions to predicting SA. This result differs somewhat from prior research showing that when BPD diagnosis, aggression, impulsivity, and childhood abuse are considered together, childhood abuse (and marginally aggression), are significant predictors of SA (Brodsky et al., 2001). This difference may be due to differences in the samples studied, as the earlier study examined depressed psychiatric inpatients, whereas this study focused on research volunteers among whom personality disorders and aggression were prevalent. Another prior study found that when considering BPD diagnosis, substance use disorder, and aggression as simultaneous predictors of completed suicide, BPD, but not aggression, was significantly associated with completed suicide among men with major depression (Dumais et al., 2005), similar to the current findings.

Research suggests that chronic adverse circumstances in childhood are associated with neurobiological alterations (Cicchetti & Toth, 2005; Lee, 2005; Watts-

English et al., 2006), which may in part explain the association with negative outcomes in adulthood, including psychopathology, aggression, and suicidal behavior. Prior research suggests that impulsive aggressive traits are influenced by both genetic and environmental factors. The present results suggest that physical and emotional abuse may constitute environmental risk factors for the development of aggression and impulsivity. In addition to neurobiological sequelae of CM, early physical abuse has been associated with biases in social information processing (Dodge et al., 1990), including the tendency to perceive hostile intentions by others, and this bias has been shown to explain the relationship between physical abuse and aggressive behavior in children. More broadly, our results are consistent with prior research showing that abuse in childhood in general and sexual abuse in particular is associated with diverse negative effects on affective, behavioral, and social functioning (Brown, Cohen, Johnson, & Smailes, 1999; Dube et al., 2005; Neumann, Houskamp, Pollock, & Briere, 1996) including disturbances in both emotional and behavioral self-regulation (Cloitre et al., 2009; van der Kolk, Perry, & Herman, 1991).

Strengths of the study include the large sample size and the psychiatrically diverse nature of the sample, permitting broader generalization than would be possible if studying a single disorder. Participants were also well-characterized with regard to Axis I and II DSM disorders and other life history and personality variables. Limitations of the study include: (1) the use of a sample of research volunteers; (2) the cross-sectional nature of the study assessments; and (3) the retrospective assessment of CM. Although the sample was comprised of research volunteers (as opposed to patients seeking treatment), the majority had a history of either formal treatment for psychiatric

disorder or of behavioral disturbance that should have been assessed by mental health professionals. Thus, the subjects seen in this study were likely similar to those seen in a treatment setting. With regard to the study design, the present results must be interpreted in light of the fact that assessments of CM, psychiatric diagnoses, and impulsive aggression were made at a single time point. As a result, it is not possible to draw strong conclusions about causal relationships from the present data. It has been suggested, for example, that children with difficult temperaments elicit harsher treatment from caretakers. However, prior research has found that the effects of child abuse on subsequent aggressive behavior remain significant even when taking into account child temperament (Dodge et al., 1990). Finally, with regard to the retrospective assessment of childhood maltreatment, the CTQ has been shown to have good validity and reliability in both clinical and non-clinical populations (Bernstein, 1994; 1998; Martin-Soelch, 2001; Scher, 2001). In the current sample, correlations between age and CTQ subscales were small ($rs < .14$), suggesting that age accounted for less than 2% of the variance in CTQ scores. This suggests there was no systematic relationship between age and reporting of CM. In spite of this, age was included as a covariate in logistic regression analyses. Finally, CTQ scores showed strong correlations with an interview measure (E.F. Coccaro, in preparation) assessing exposure to physical aggression (CTQ physical abuse: $r=.55$, $p<.001$) and verbal aggression (CTQ emotional abuse: $r=.60$, $p<.001$) in childhood and adolescence.

The present results suggest that physical abuse in childhood is a specific risk factor for the development of IED and that sexual and emotional abuse are specific risk factors for suicide attempt. Impulsive and aggressive traits largely account for the

relationship between physical abuse in childhood and IED diagnosis, and between emotional abuse in childhood and suicide attempt. Sexual abuse was strongly associated with suicide attempt independent of the effects of impulsivity and aggression. In this way, these data lend support the recently proposed Research Domain Criteria (RDoC) approach to the study of dimensions of behavior, rather than simply examining diagnostic entities alone (Insel et al., 2010).

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FINANCIAL DISCLOSURES

Dr. Coccaro reports being on the Scientific Advisory Board of Azevan Pharmaceuticals, Inc.; Dr. Lee reports being the recipient of a research grant from Azevan Pharmaceuticals, Inc. Neither Dr. Fanning nor Mr. Meyeroff report any conflicts of interest.

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Table 1

Demographic Characteristics of the Sample

	HC (N = 185)	PC (N = 199)	IED (N = 264)	p-value	SA- (N=586)	SA+ (N=62)	p-value
Age (Years)	30.4 ± 8.4	33.4 ± 9.7	37.0 ± 10.0	<.001[1]	33.7 ± 9.8	36.7 ± 9.9	<.05[1]
Gender (n: M / F)	104 / 81	127 / 72	142 / 122	NS[2]	353 / 233	20 / 42	<.001[2]
Race (n: White /Other)	116 / 69	114 / 85	139 / 125	NS[2]	336 / 250	33 / 29	NS[2]
SES Class (n: I / II / III / IV / V)	23 / 74 / 36 / 27 / 25	18 / 53 / 49 / 39 / 40	26 / 103 / 54 / 49 / 32	NS[1]	61 / 211 /122 / 104 / 88	6 / 19 / 17 / 11 / 9	NS[1]

HC = Healthy Control, PC = Psychiatric Control, IED = Intermittent Explosive Disorder; SA- = No Suicide Attempt; SA+ = Suicide Attempt

[1] Significance following ANOVA. Post-hoc (Games-Howell) for Age: HC < PC < IED (p<.01)

[2] Significance following Fisher's Exact Test

TABLE 2

Comorbid Axis I and Personality Disorders in Psychiatric Control and Intermittent Explosive Disorder Subjects

	PC (N = 199)	IED (N = 264)	Odds	SA- (NA = 586)	SA+ (NA = 62)	Odds
	n (%)	n (%)	OR (95% CI)	n (%)	n (%)	OR (95% CI)
Lifetime Syndromal Disorders:						
Intermittent Explosive Disorder	0 (0%)	264 (100%)	--	219 (37.4%)	34 (72.6%)	2.0 (1.2-3.6)[1]
Any Depressive Disorder	63 (31.7%)	169 (64.4%)	3.8 (2.6-5.8)[2]	180 (30.7%)	52 (83.9%)	11.7 (5.7-26.4)[2]
Any Anxiety Disorder	23 (11.6%)	69 (26.1%)	2.7 (1.6-4.7)[2]	74 (12.6%)	18 (29.0%)	2.8 (1.5-5.3)[1]
Any Trauma/Stress Disorders	24 (12.1%)	50 (18.9%)	1.7 (1.0-3.0)[ns]	55 (9.4%)	21 (33.9%)	4.9 (2.6-9.3)[2]
Any Obsessive-Compulsive Disorder	4 (2.0%)	10 (3.8%)	1.9 (0.5-8.5)[ns]	13 (2.2%)	1 (1.6%)	0.7 (0.0-5.0)[ns]
Any Substance Use Disorder	75 (37.7%)	156 (59.1%)	2.4 (1.6-3.5)[2]	197 (33.6%)	37 (59.7%)	2.9 (1.7-5.2)[2]
Eating Disorder	9 (4.5%)	25 (9.5%)	2.2 (1.0-5.5)[1]	28 (4.8%)	6 (9.7%)	2.1 (0.7-5.6)[ns]
Somatoform Disorder	1 (0.5%)	5 (1.9%)	3.8 (0.4-180.5)[ns]	5 (0.9%)	1 (1.6%)	1.9 (0.0-17.4)[ns]
Personality Disorders:						
Cluster A	17 (8.5%)	47 (17.8%)	2.3 (1.3-4.5)[1]	49 (8.4%)	15 (24.2%)	3.5 (1.7-6.9)[2]
Cluster B	39 (19.6%)	127 (48.1%)	3.8 (2.4-6.0)[2]	127 (21.7%)	39 (62.9%)	6.1 (3.4-11.1)[2]
Cluster C	35 (17.6%)	72 (27.8%)	1.8 (1.1-2.9)[1]	83 (14.2%)	24 (38.7%)	3.8 (2.1-6.9)[2]

[1] p<.05; [2] p<.001; [ns] = non-significant; PC = Psychiatric Control subjects; IED = Intermittent Explosive Disorder subjects; SA- = non-suicide attempters; SA+ = suicide attempters.

TABLE 3

CTQ Subscales Scores as a Function of Psychiatric Group and Suicide-Attempters versus Non-Attempters (Mean ± SD)

	HC (n=185)	PC (n=199)	IED (n=264)	Group Differences	SA- (n=586)	SA+ (n=62)	Group Differences
Physical Abuse	6.5 ± 2.3	8.2 ± 3.9	10.1 ± 4.8	HC < PC < IED[1]	8.2 ± 4.0	11.2 ± 5.2	SA- < SA+[2]
Sexual Abuse	5.6 ± 2.1	7.0 ± 4.5	7.9 ± 5.4	HC < PC < IED†	6.5 ± 3.7	11.5 ± 7.6	SA- < SA+[2]
Emotional Abuse	8.3 ± 3.2	11.0 ± 4.5	12.8 ± 5.0	HC < PC < IED[1]	10.5 ± 4.5	15.2 ± 5.5	SA- < SA+[2]
Physical Neglect	5.8 ± 1.5	7.1 ± 2.8	8.1 ± 3.4	HC < PC < IED[1]	7.0 ± 2.7	9.0 ± 3.9	SA- < SA+[2]
Emotional Neglect	9.0 ± 4.1	11.5 ± 5.0	13.2 ± 5.4	HC < PC < IED[1]	11.1 ± 5.1	15.1 ± 5.2	SA- < SA+[2]
LHA Aggression	5.4 ± 3.9	8.3 ± 5.2	18.0 ± 4.4	HC < PC < IED[1]	10.9 ± 7.0	16.7 ± 5.9	SA- < SA+[2]
BIS Impulsivity	55.9 ± 8.8	62.5 ± 10.1	68.7 ± 11.1	HC < PC < IED[1]	62.2 ± 11.0	72.5 ± 11.6	SA- < SA+[2]

[1] Omnibus test significant at p<.001, Games-Howell (G-H) post hoc test significant at p<.01; [2] t-test significant at p<.001; HC = Healthy Control; † Omnibus test significant at p< .001, G-H test p<.10; PC = Psychiatric Control; IED = Intermittent

Explosive Disorder; SA- = No suicide attempt history; SA+ = History of suicide attempt; LHA = Life History of Aggression Scale; BIS = Barratt Impulsivity Scale (11th Ed.)

TABLE 4

Bivariate correlations between childhood trauma, aggression, and impulsivity

	1	2	3	4	5	6	7
1. Physical Abuse	**.84**						
2. Sexual Abuse	.40	**.95**					
3. Emotional Abuse	.66	.36	**.90**				
4. Physical Neglect	.55	.35	.61	**.76**			
5. Emotional Neglect	.52	.31	.71	.67	**.93**		
6. LHA Aggression	.37	.20	.36	.29	.31	**.88**	
7. BIS Impulsivity	.28	.18	.36	.28	.31	.44	**.87**

All *p*s < .001; Cronbach's alpha for each scale is reported on the diagonal.

TABLE 5A

Predictors of Intermittent Explosive Disorder Diagnosis

	Model 1			Model 2			Model 3			Model 4		
	β	**Wald χ^2**	**OR (95% CI)**	**β**	**Wald χ^2**	**OR (95% CI)**	**β**	**Wald χ^2**	**OR (95% CI)**	**β**	**Wald χ^2**	**OR (95% CI)**
Step 1	**Δ χ2(4)=46.0**		**p<.001**									
Age	0.04	22.4**	1.0 (1.0-1.1)	0.05	11.5*	1.0 (1.0-1.1)	0.05	21.7**	1.0 (1.0-1.1)	0.05	12.4**	1.1 (1.0-1.1)
Gender	0.19	1.0	1.2 (0.8-1.7)	0.43	2.3	1.5 (0.9-2.7)	0.13	0.4	1.1 (0.8-1.7)	0.49	2.6	1.6 (0.9-2.9)
Race	0.10	0.3	1.1 (0.7-1.6)	0.09	0.1	1.1 (0.6-1.9)	-0.04	0.0	1.0 (0.6-1.4)	-0.06	0.0	0.9 (0.5-1.7)
SES	0.01	0.7	1.0 (1.0-1.0)	0.01	1.5	1.0 (1.0-1.0)	0.01	0.9	1.0 (1.0-1.0)	0.01	1.5	1.0 (1.0-1.0)
Step 2[a]	**Δ χ2(5)=67.5**		**p<.001**									
Emotional Abuse	0.24	2.8[†]	1.3 (1.0-1.7)	0.03	0.0	1.0 (0.7-1.6)	0.07	0.2	1.0 (0.8-1.5)	-0.06	0.1	0.9 (0.6-1.5)
Physical Abuse	0.37	8.5**	1.5 (1.1-1.9)	0.00	0.0	1.0 (0.7-1.4)	0.34	5.8*	1.4 (1.0-1.9)	0.05	0.1	1.1 (0.7-1.6)
Emotional Neglect	0.13	0.9	1.1 (0.9-1.5)	0.12	0.3	1.1 (0.8-1.7)	0.18	1.5	1.2 (0.9-1.6)	0.14	0.5	1.2 (0.8-1.7)
Physical Neglect	0.10	0.6	1.1 (0.9-1.4)	-0.02	0.0	1.0 (0.7-1.4)	-0.02	0.0	1.0 (0.7-1.3)	-0.09	0.2	0.9 (0.6-1.4)
Sexual Abuse	0.07	0.5	1.1 (0.9-1.3)	0.00	0.0	1.0 (0.8-1.3)	0.05	0.2	1.0 (0.8-1.3)	-0.03	0.0	1.0 (0.7-1.3)
Step 3							**Δ χ2(2)=85.8**		**p<.001**			

Antisocial PD							2.4	29.4**	10.9 (4.6-26.0)	1.56	6.5*	4.8 (1.4-15.8)
Borderline PD							1.7	25.8**	5.4 (2.8-10.3)	0.61	2.0	1.8 (0.8-4.3)
Step 4[ab]				**Δ χ2(2)=387.3**		**p<.001**				**Δ χ2(2)=312.4**		**p<.001**
Aggression				2.64	144.1**	14.0 (9.1-21.5)				2.60	135.1**	13.1 (8.5-20.2)
Impulsivity				0.44	8.5*	1.6 (1.2-2.1)				0.30	3.6†	1.4 (1.0-1.9)

* p < .05; ** p < .001; † < .10; [a] Variables in this step were z-transformed; [b] In Model 2 aggression and impulsivity were entered in Step 3. Model 1 shows the relationship between subtypes of childhood maltreatment and IED diagnosis. Model 2 shows how adding aggression and impulsivity to the model affects the relationship between CM and IED diagnosis. Model 3 shows the relationship between CM and IED, controlling for antisocial and borderline personality disorders. Model 4 shows the relationships when all variables are included in the model.

TABLE 5B

Predictors of Suicide Attempt

	Model 1			Model 2			Model 3			Model 4		
	β	**Wald χ^2**	**OR (95% CI)**	**β**	**Wald χ^2**	**OR (95% CI)**	**β**	**Wald χ^2**	**OR (95% CI)**	**β**	**Wald χ^2**	**OR (95% CI)**
Step 1	**Δ χ2(4)=24.6**		**p<.001**									
Age	0.02	1.7	1.0 (1.0-1.0)	0.01	0.6	1.0 (1.0-1.0)	0.02	1.3	1.0 (1.0-1.1)	0.01	0.7	1.0 (1.0-1.0)
Gender	0.89	7.9*	2.4 (1.3-4.5)	0.93	7.6*	2.5 (1.3-4.9)	0.81	5.5*	2.2 (1.1-4.4)	0.84	5.5*	2.3 (1.1-4.6)
Race	-0.31	0.9	0.7 (0.4-1.4)	-0.38	1.2	0.7 (0.3-1.4)	-0.52	2.1	0.6 (0.3-1.2)	-0.47	1.6	0.6 (0.3-1.3)
SES	-0.01	0.3	1.0 (1.0-1.0)	0.00	0.0	1.0 (1.0-1.0)	0.00	0.3	1.0 (1.0-1.0)	0.00	0.0	1.0 (1.0-1.0)
Step 2[a]	**Δ χ2(5)=54.8**		**p<.001**									
Emotional Abuse	0.56	6.1*	1.7 (1.1-2.7)	0.33	2.0	1.4 (0.9-2.2)	0.38	2.6	1.5 (0.9-2.3)	0.29	1.5	1.3 (0.8-2.1)
Physical Abuse	-0.12	0.4	0.9 (0.6-1.3)	-0.18	0.9	0.8 (0.6-1.2)	-0.13	0.5	0.9 (0.6-1.3)	-0.17	0.8	0.8 (0.6-1.2)
Emotional Neglect	0.18	0.7	1.2 (0.8-1.8)	0.18	0.6	1.2 (0.8-1.9)	0.23	1.1	1.3 (0.8-2.0)	0.20	0.8	1.2 (0.8-1.9)
Physical Neglect	-0.05	0.1	0.9 (0.7-1.3)	-0.07	0.1	0.9 (0.7-1.3)	-0.17	0.9	0.8 (0.6-1.2)	-0.14	0.6	0.9 (0.6-1.2)
Sexual Abuse	0.50	17.8**	1.6 (1.3-2.1)	0.52	17.5**	1.7 (1.3-2.1)	0.55	18.9**	1.7 (1.4-2.2)	0.55	18.0**	1.7 (1.3-2.2)

Step 3							**Δ χ2(2)=25.1**		**p<.001**			
Antisocial PD							0.99	5.3*	2.7 (1.2-6.3)	0.51	1.3	1.7 (0.7-4.0)
Borderline PD							1.24	13.0**	3.5 (1.8-6.8)	0.85	5.7*	2.3 (1.2-4.7)
Step 4[ab]				**Δ χ2(2)=29.0**		**p<.001**				**Δ χ2(2)=11.9**		**p<.01**
Aggression				0.45	5.7*	1.6 (1.1-2.3)				0.32	2.6	1.4 (0.9-2.0)
Impulsivity				0.63	13.6**	1.9 (1.3-2.6)				0.48	6.9*	1.6 (1.1-2.3)

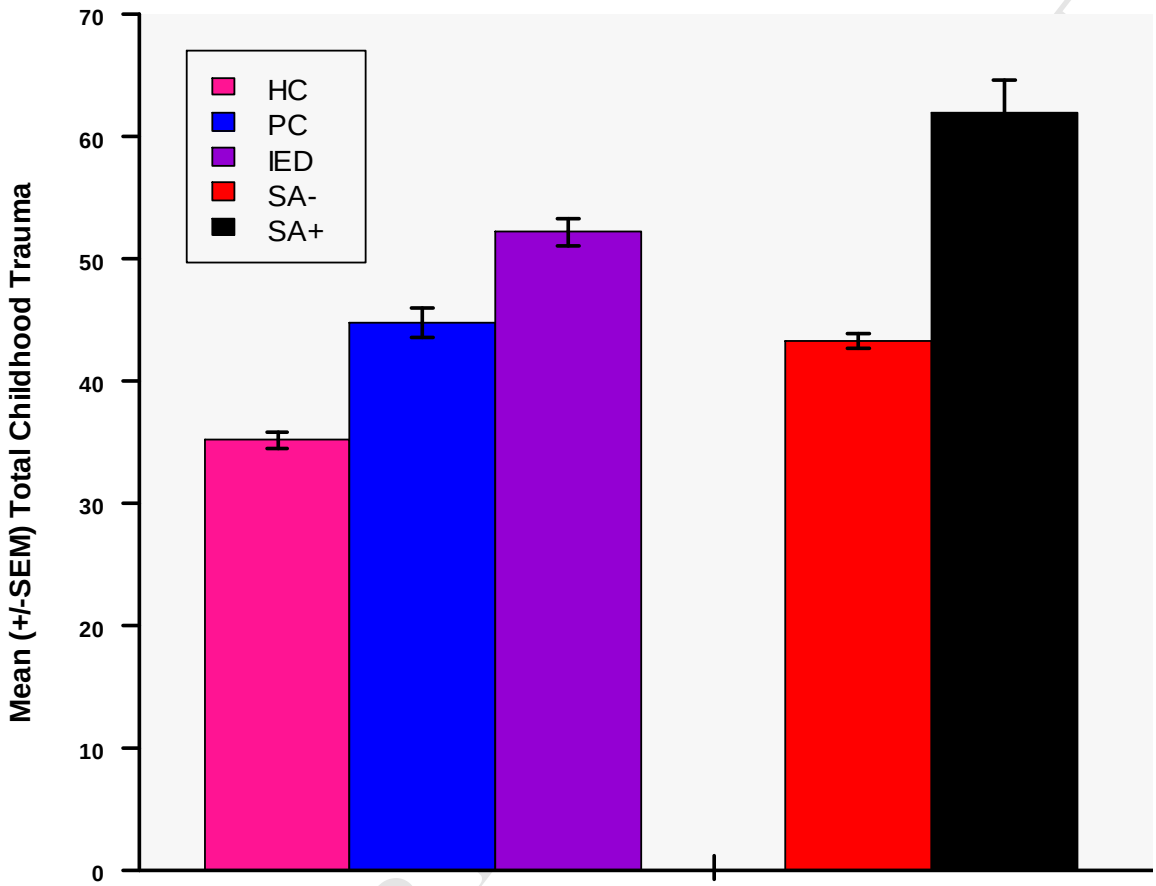
* p < .05; ** p < .001; † < .10; [a] Variables in this step were z-transformed; [b] In Model 2 aggression and impulsivity were entered in Step 3. Model 1 shows the relationship between subtypes of childhood maltreatment and suicide attempt (SA). Model 2 shows how adding aggression and impulsivity to the model affects the relationship between CM and SA. Model 3 shows the relationship between CM and SA, controlling for antisocial and borderline personality disorders. Model 4 shows the relationships when all variables are included in the model.

Figure Legends:

Figure 1:

Left: Mean (+ SEM) Total CTQ Scores among HC/PC/IED groups; all groups differ at p <.001. Right: Mean (+ SEM) Total CTQ Scores among non-suicide attempters (SA-) and suicide attempters (SA+)

Figure 1



CONFLICT OF INTEREST STATEMENT:

Dr. Coccaro reports being on the Scientific Advisory Board of Azevan Pharmaceuticals, Inc. and being a current recipient of grants from the NIMH. Dr. Lee reports being a past recipient of a research grant from Azevan Pharmaceuticals, Inc. Neither Dr. Fanning, nor Mr. Meyeroff, report any conflict of interest regarding this work.

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