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Psychiatric comorbidity in Intermittent Explosive Disorder

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ABSTRACT

This study examined aspects of psychiatry comorbidity in Intermittent Explosive Disorder (IED) in order to explore the validity of IED in the context of other psychiatric disorders. Data from the National Comorbidity Study – Revised (NCS-R: n = 9,282 adults) and its Adolescent Supplement (NCS-AS: n = 10,148 adolescents) and a large clinical research data set (n = 1640) were analyzed in this study. Mean number of comorbid disorders among current IED participants was similar to that among other Non-IED disorders and comorbidity of IED with Non-IED disorders was similar to comorbidity among Non-IED disorders. When examined together, current IED was significantly comorbid with current bipolar, depressive, anxiety, substance use, and post-traumatic stress disorder, and age of onset of IED generally preceded that of the comorbid disorders. Finally, mean aggression scores were generally highest among those with IED and the comorbid disorder while scores among those with the comorbid disorder alone were generally less than that with IED or with IED and the comorbid disorder. Comorbidity in IED is similar to that in other, more established, Non-IED disorders. The observation that the development of IED precedes the onset of most comorbid disorders and that aggression scores in those with IED and a comorbid disorder are often higher than those with IED alone supports the rationale that a diagnosis of both IED and the comorbid disorder should be made when both are present.

1. Introduction

Impulsive aggressive behavior appears in psychiatric patients with diagnoses ranging from schizophrenia and other psychotic disorders, bipolar disorders, unipolar depressive and anxiety disorders, substance use disorders, post-traumatic stress, and eating disorders, among others. For this reason, clinicians have been reluctant to make the diagnosis of IED in the presence of other psychiatric diagnoses (Coccaro, 2012; Zapata and Palacio, 2016). In the DSM-III (American Psychiatric Association, 1980), the diagnosis of IED was a disorder of exclusion and the presence of almost any other psychiatric disorder ruled out a diagnosis of IED.

Later, DSM-IV (American Psychiatric Association, 1994) revised IED criteria by relaxing these comorbidity exclusions so that IED could be diagnosed provided that another psychiatric disorder did not "better explain" the aggressiveness of the individual in question. Later, Research Diagnostic Criteria (Coccaro, 2011; Coccaro et al., 1998) and DSM-5 Diagnostic Criteria (American Psychiatric Association, 2013) formalized this by stating that IED could be diagnosed along with other disorders provided that the individual also met criteria for IED at times in the absence of comorbid disorders or when a comorbid disorder did not better explain the aggressive behavior. Expanding the diagnostic reach of IED, however, has the drawback of making the disorder unrealistically prevalent and making it open to the criticism that IED may now occur in the context of so many other disorders that it is not a robust enough construct to constitute a disorder of impulsive aggression.

In this paper, we examine the issue of psychiatric comorbidity in IED based on available empiric data from two large community surveys and from a relatively large clinical research data set. We examine the nature of overall and specific comorbidity of IED, as well as the relative ages of onset of IED and that of its comorbid disorders. Because the reliability of all diagnoses is highest when considering the current (i.e., past year) presence of these disorders, we focused on current comorbidity for most analyses. Finally, we also examine the quantitative nature of aggression scores as a function of lifetime IED and its lifetime comorbid conditions. Based on the literature we were most interested in examining the comorbidity of current IED with current bipolar (McElroy et al., 1998), depressive (Fava and Leibenluft, 2019; Medeiros et al., 2018), anxiety (Keyes et al., 2016), substance use (Coccaro et al., 2016, 2017), post-traumatic stress (Fanning et al., 2016; Reardon et al., 2014), and bulimic/binge eating (Fernandez-Aranda et al., 2006;

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Jennings et al., 2017), disorders. We hypothesized that while current IED would display an increased rate of these comorbid disorders, individuals with IED would display: a) no more overall current comorbidity than these other Non-IED disorders, b) ages of onset that would precede that of each comorbid disorders and, c) similarly high aggression scores in those with IED alone and in those with IED and another comorbid disorder and higher aggression scores in those with the comorbid disorder only. If so, these data would support the overall hypothesis that IED is a disorder in its own right and is not due to the presence of other disorders.

2. Methods

This study used cross-sectional data from two community samples [National Comorbidity Survey – Replication (NCS-R; n = 9,282) and the National Comorbidity Survey – Adolescent Supplement (NCS-AS; n = 10,148)] and our own clinical research sample (n = 1,642). This study was approved by the University of Chicago Institutional Review Board.

2.1. Study samples

2.1.1. Community samples

The NCS-R and NCS-R-AS are nationally representative surveys of the prevalence and correlates of mental disorders in the United States of America. Fully structured and laptop computer-assisted interviews were administered face-to-face to a sample of adolescents (NCS-AS) and adults (NCS-R) who were English-speaking and living in the non-institutionalized civilian household population of the coterminous US (excluding Alaska and Hawaii) between 2001 and 2004. Details regarding the design and acquisition of the two NCS-R samples have been published (Kessler et al., 2009; Kessler and Merikangas, 2004). NCS-AS participants were predominantly white (74.6%) males (48.9%) and females (55.1%), with a mean age of 15.8 ± 1.5 years, and with parents who had no more than a high school degree (41.6%), had attended college (25.2%), or had a college degree or higher (33.2%); NCS-R participants were predominately white (72.1%) males (44.6%) and females (55.4%), with a mean age of 44.7 ± 17.5 years who had no more than a high school degree (40.5%), had attended college (29.4%), or had a college degree or higher (30.1%). While the NCS-AS and the NCS-R studies were designed to assign DSM-IV (American Psychiatric Association, 1994) diagnoses, raw data enabled an updating of DSM-IV to DSM-5 (American Psychiatric Association, 2013) diagnoses. For the diagnosis of IED, participants reported at least three "anger attacks" in any given year (Criteria A_2); while DSM-5 criteria also allow frequent, though low intensity "anger attacks" (Criteria A_1), neither interview schedule used in the NCS-R or NCS-AS survey included questions that allowed for the assessment of these types of "anger attacks". In addition, "anger attacks" were out of proportion to the circumstances in which they occurred (Criteria B); impulsive/anger-based in nature (Criteria C); associated with functional impairment and/or distress (Criteria D); and had "anger attacks" not better explained by other factors or other psychiatric disorders (Criteria F); finally, all participants were at least six years of age (Criterion E). Psychiatric disorders examined in this study included bipolar disorder (bipolar I and bipolar II), depressive disorder (major depression and persistent depressive disorder), phobic (agoraphobia, social phobia, specific phobia) and non-phobic (panic disorder and general) anxiety disorders, substance use disorder (all types), post-traumatic stress disorder, and relevant eating disorders (bulimia and binge eating disorder).

2.1.2. Clinical research sample

The majority of the Clinical Research sample participants were white (54.3%; 33.7% African-American; 12.1% Other), male (56.4%) and female (43.6%), with a mean age of 33.3 ± 9.9 years and up to a high school degree (33.2%), partial college (28.8%), and a college degree or higher (33.0%). Details regarding the clinical research sample have been published (Coccaro et al., 2016). Psychiatric diagnoses were made using DSM-5 criteria (Amercian Psychiatric Association, 2013). DSM-5 diagnoses were based on information obtained from: (a) the Structured Clinical Interview for DSM Diagnoses (SCID-I; First et al., 1997, 2014), (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 psychology or social work after a rigorous training program including lectures on DSM diagnoses and rating systems, videos of expert raters conducting SCID interviews, and practice interviews/ratings until the raters were deemed reliable with the trainer. This process resulted in good to excellent inter-rater reliabilities (mean kappa = 0.84 ± 0.05; range: 0.79–0.93) across mood, anxiety, substance use, post-traumatic stress, and eating, disorders. Final DSM-5 diagnoses were assigned by team best-estimate consensus procedures involving research psychiatrists and clinical psychologists as previously described (Coccaro et al., 2016). Unlike the NCS-AS and the NCS-R surveys, individuals in the Clinical Research group were assessed for the A_1 criterion for DSM-5 IED. The psychiatric disorders examined in this group included those noted above with the addition of depressive disorder-not otherwise specified in the depressive disorder group and anxiety disorder-not otherwise specified in the non-phobic anxiety disorder group. For participants with any psychiatric diagnosis (n = 1,189), 58% (n = 690) reported a history of formal psychiatric evaluation and/or treatment, and 14% (n = 166) reported a history of behavioral disturbance during which the subject or others thought they should have sought mental health services but did not.

2.2. Behavioral variables relevant to IED

Both the NCS-AS and NCS-R surveys included questions regarding various dimensions of personality (45 items for NCS-AS; 44 items for NCS-R) some of which were relevant to IED (aggression and/or impulsivity). In each community sample, six (6) items were relevant to aggression and impulsivity allowing the creation of an impulsive aggression variable. Examples of these items for the NCS-AS included: "I have a very strong temper", "When people shout at me I shout back", "I often do things without thinking of the consequences" (alpha coefficient = 0.73). Examples of the NCS-R items included: "I have tantrums or angry outbursts", "I lose my temper and get into physical fights", "I take chances and do reckless things" (alpha coefficient = 0.68). The Clinical Research data set assessed relevant variables and included the Aggression score from the Life History of Aggression (LHA) assessment (Coccaro et al., 1997) as well as the Aggression score from the Buss-Perry Aggression Questionnaire (BPAQ; Buss and Perry, 1992). Psychometric properties of both the LHA and BPAQ are good to excellent. While both scores reflect aggressiveness, each display a nearly large-sized relationship with measures of impulsivity (e.g., Barratt Impulsiveness Scale (Patton et al., 1995) scores and LHA: r = 0.42; BPAQ: r = 0.44, both $p < 0.001$).

2.3. Statistical analysis

Statistical procedures included binary logistic regression for adjusted odds ratios, analysis of covariance (ANCOVA), and paired t-tests, as appropriate. All reported data was adjusted for age, sex, ethnicity, and education (level for parent for NCS-AS; level for subject for NCS-R) or Hollingshead Socio-Economic Status score (Clinical Research sample). A two-tailed alpha of 0.05 was used to denote statistical significance for all analyses. The first set of analyses involved examined the number of current disorders for each sample. This was followed by an examination of the rates (percentages) and risk (odds ratio) for overall comorbidity (e.g., comorbidity of a disorder with all other disorders). Next, we examined the rates and comorbidity risk for each Non-IED disorder as a function of IED taken separately as well as

examining the comorbidity risk for all disorders in the same statistical model to determine the true comorbid nature of IED. The second set of analyses examined the age (and relative sequence) of onset for IED and each comorbid disorder to determine the temporal nature of IED comorbidity. The third set of analyses examined mean composite aggression scores as a function of comorbidity. For example, subjects in each sample were divided into those with no life history of any disorder, those with the comorbid disorder of interest (e.g., Depressive Disorder), those with other comorbid disorders (e.g., all other Non-IED Disorders), those with only IED, and those with IED and the comorbid disorder of interest. This was performed to determine if aggression/impulsivity scores were higher in IED Alone compared with those with the comorbid disorder of interest (e.g., Depressive Disorder) and compared with both IED Alone and the comorbid disorder of interest (e.g., IED + Depressive Disorder). Composite Aggression scores were created for the NCS-AS and NCS-R groups by taking the mean z scores of the aggression/impulsivity items and the "greatest number of anger attacks in any year" (after log-transformation). Composite Aggression scores were created for the Clinical Research data set by taking the mean z scores for LHA Aggression and BDHI Aggression scores.

3. Results

3.1. Current comorbidity across all disorders

Except for phobic anxiety disorder, the mean number of current disorders reported for all study participants ranged between two and three disorders. The number of current comorbid disorders for IED was statistically the same as that for bipolar disorder, non-phobic anxiety disorder, post-traumatic stress disorder, and bulimia/binge eating disorders, with IED having significantly fewer comorbid disorders compared with depressive disorder, substance use disorder, and phobic anxiety disorder (Supplemental Table 1).

3.2. Overall comorbidity for IED and Non-IED disorders (Table 1)

While overall comorbidity for IED was moderately high in both community samples, its comorbidity with other disorders was lower than that for bipolar disorder, post-traumatic stress disorder, non-phobic anxiety disorder, and bulimia/binge eating disorder and about the same for depressive disorder, substance use disorder, and phobic anxiety disorder. The rate of overall comorbidity of current IED in the Clinical Research sample was lowest among all other disorders. Odds ratios for overall comorbidity for current bipolar disorder (NCS-R), current non-phobic anxiety disorder (NCS-AS/NCS-R), and current post-traumatic stress disorder (NCS-AS/NCS-R), were each significantly higher than that for current IED; this was also true for the Clinical Research sample for current non-phobic anxiety disorder and current post-traumatic stress disorder compared with that for current IED.

3.3. Comorbidity of current IED with specific current disorders (Table 2)

Across the two community samples, the most frequent current disorder comorbid with IED was phobic anxiety disorder (37.7–50.3%), followed by depressive disorder (18.8–19.0%), substance use disorder (14.0–23.7%), non-phobic anxiety disorder (10.0–22.2%), post-traumatic stress disorder (8.2–13.5%), bipolar disorder (6.9–8.7%), and bulimia/binge eating disorder (1.9–3.5%) In the Clinical Research sample depressive disorder was the most frequent comorbid disorder (21.1%), followed by phobic anxiety disorder (12.4%), non-phobic anxiety disorder (11.9%), post-traumatic stress disorder (11.1%), and bulimia/binge eating disorder (2.9%). Odds ratios for current IED comorbidity were substantial, and statistically significant, for nearly all disorders (except for bulimia/binge eating disorder in the NCS-R sample). For the community samples, odds ratios ranged from 3.17 to 4.39 for the NCS-AS sample and from 2.62 to 5.38 for the NCS-R sample. In the Clinical Research sample, odds ratios were lower in magnitude, ranging from 1.70 to 4.42 and elevated by a statistically significantly degree for each disorder.

3.4. Comorbidity in the context of all disorders (Table 3)

Given the substantial comorbidity of each examined disorder with other disorders we placed all current disorders into the same logistic regression model (one model per sample) to determine which disorders had significantly elevated odds ratios for IED comorbidity considering the comorbidity among all Non-IED disorders. Results across the three samples were consistent. Bipolar disorder displayed a significantly elevated odds ratio for IED in the two samples where this data was available, as did depressive disorder, though not in the NCS-R sample. Non-phobic anxiety disorder and post-traumatic stress disorder displayed significantly elevated odds ratios for IED in all three samples while substance use disorder displayed elevated odds ratios for IED in the two samples where this data was available. In contrast, bulimia/binge eating disorder did not display a significantly elevated odds ratio for IED in any sample. Performing these analyses with the Non-IED disorders (e.g., Depressive Disorder rather than IED) revealed the same (i.e., significantly elevated odds ratios for all Non-IED disorders for nearly all other disorders).

3.5. Age of onset and temporal order of IED and comorbid disorders (Table 4)

Across the three samples, IED displayed an earlier reported age of onset compared with its comorbid disorder in almost all examined disorders. For the Adolescent NCS-AS sample, however, age of onset for any anxiety disorder preceded that for IED and age of onset for post-traumatic stress disorder was similar to that for IED. The same result was found when examining age of onset as a function of IED occurring first, second, or at the same time as, the co-morbid disorder (Supplemental Table 2).

3.6. Magnitude of aggression/impulsivity scores as a function of comorbidity (Table 5)

Finally, comparing levels of aggression/impulsivity as a function of comorbidity (i.e., No Disorder *vs*. Other Disorder *vs*. Comorbid Disorder *vs*. IED Alone *vs*. IED + Comorbid Disorder) found that composite aggression scores were higher for the "Comorbid Disorder" alone compared with both "Other Disorder" and "No Disorder" controls and that aggression scores were highest for those with "IED Alone" or "IED + Comorbid Disorder". In the community samples, the combined IED + Comorbid disorder group typically displayed higher aggression scores than the IED alone group; this was not true in the clinical research data set where scores were similar between IED + Comorbid disorder and IED alone groups, with the exception of PTSD where the combined group had the highest aggression scores.

4. Discussion

Analysis of data from three different samples strongly suggest that, with few exceptions: a) the mean number of comorbid disorders in those with current DSM-5 IED is similar to (or less than) the mean number of comorbid disorders among current Non-IED disorders; b) any current comorbidity of IED with current Non-IED disorders is similar to (or less than) any current comorbidity those with current Non-IED disorders; c) taking all examined disorders simultaneously, current IED is significantly comorbid with current bipolar, depressive, anxiety substance use, and post-traumatic stress, disorder; d) the age of onset of IED precedes that of all other examined disorders with the exception of phobic anxiety disorders; and, e) mean aggression/impulsivity scores are highest among those with IED and those with IED + Comorbid

Table 1
Overall comorbidity of current IED compared with that of other current disorders.

With vs. Without Disorder	NCS-AS Reanalysis OR (95% CI) [% Dx vs. % Other-Dx]	NCS-R Reanalysis OR (95% CI) [% Dx vs. % Other-Dx]	Clinical Research Analysis OR (95% CI) [% Dx vs. % Other Dx]
IED vs. All Other Dx	4.93 (4.03–5.99) [67.6% vs. 30.7%]	5.68 (4.31–7.52) [66.4% vs. 23.8%]	2.67 (2.11–3.37) [39.5% vs. 18.8%]
Bipolar Dx vs. All Other Dx	8.13 (5.68–11.63) [80.6% vs. 32.6%]	24.39 (13.89–43.48) [89.9% vs. 24.6%]	N/A
Depressive Dx vs. All Other Dx	4.72 (4.02–5.52) [67.1% vs. 28.5%]	6.90 (5.85–8.13) [64.5% vs. 19.3%]	3.88 (2.83–5.29) [72.8% vs. 39.2%]
Non-Phobic Dx vs. All Other Dx	8.00 (5.99–10.75) [80.2% vs. 32.0%]	11.63 (9.52–14.29) [76.3% vs. 21.0%]	5.75 (3.56–9.26) [82.5% vs. 43.5%]
Phobic Dx vs. All Other Dx	4.05 (3.64–4.50) [38.1% vs. 13.0%]	7.35 (6.49–7.87) [60.1% vs. 16.5%]	3.90 (2.67–5.71) [73.2% vs. 42.4%]
SUD vs. All Other Dx	3.95 (3.26–4.85) [62.9% vs. 31.0%]	5.56 (4.59–6.76) [64.2% vs. 24.5%]	N/A
PTSD vs. All Other Dx	8.47 (6.25–11.40) [81.9% vs. 32.0%]	11.90 (8.85–15.87) [82.8% vs. 26.1%]	10.87 (5.81–22.73) [91.3% vs. 44.8%]
Bulimia/Binge Eating Dx vs. All Other Dx	6.54 (4.44–9.71) [79.2% vs. 32.9%]	7.14 (3.62–14.08) [85.1% vs. 41.64%]	24.39 (3.24–166.67) [96.3% vs. 47.0%]

Table 2
Odds ratios and frequencies of current disorders Co-Morbid with current IED.

Current IED vs. Comorbid Disorder	NCS-AS Reanalysis OR (95% CI) [% Dx in IED vs. % in Non-IED]	NCS-R Reanalysis OR (95% CI) [% Dx in IED vs. % in Non-IED]	Clinical Research Analysis OR (95% CI) [% Dx in IED vs. % in Non-IED]
Bipolar Disorder	4.12 (2.80–6.06) [6.9% vs. 1.7%]	4.22 (2.99–5.99) [8.4% vs. 1.3%]	N/A
Depressive Disorder	3.17 (2.48–4.07) [19.0% vs. 7.1%]	3.04 (2.32–3.98) [22.3% vs. 7.5%]	2.07 (1.55–2.75) [21.1% vs. 10.5%]
Non-Phobic Anxiety Disorder	4.39 (3.16–6.10) [10.0% vs. 2.5%]	4.92 (3.55–6.90) [21.8% vs. 5.6%]	2.30 (1.58–3.36) [11.9% vs. 5.3%]
Phobic Anxiety Disorder	3.51 (2.91–4.24) [50.3% vs. 22.8%]	3.60 (2.75–4.78) [39.1% vs. 14.0%]	1.70 (1.20–2.39) [12.4% vs. 8.0%]
Substance Use Disorder	4.00 (2.99–5.35) [14.0% vs. 3.9%]	3.98 (3.03–5.24) [23.9% vs. 5.1%]	N/A
Post-Traumatic Stress Disorder	3.48 (2.44–4.97) [8.2% vs. 2.6%]	3.89 (2.74–5.52) [13.4% vs. 3.3%]	4.42 (2.75–7.14) [11.1% vs. 2.6%]
Bulimia/Binge Eating Disorder	2.46 (1.47–4.13) [3.5% vs. 1.5%]	3.79 (1.58–9.01) [2.5% vs. 0.7%]	2.75 (1.23–6.17) [2.9% vs. 0.9%]

disorder while scores among those with the Comorbid disorder alone less than those with IED or with IED + Comorbid disorder.

The observation that the overall comorbidity of IED is similar to that of other Non-IED disorders is noteworthy because it suggests that current IED does not display more comorbidity with other disorders than those that are considered valid psychiatric disorders for decades. In fact, the risk of other current disorders is greater in those with current bipolar, non-phobic anxiety, and post-traumatic stress, disorders (both NCS-AS and NCS-R) than it is for current IED. Equally important is the observation that, when all comorbid disorders are considered together, the odds ratios for IED comorbidity with each comorbid disorder are relatively modest in magnitude being between 1.56 (current post-traumatic stress disorder) and 2.74 (current substance use disorder) indicating that while comorbidity in IED is present with a number of disorders no psychiatric disorder, by itself, accounts for a large risk for current comorbidity.

It is also noteworthy that the addition of IED to the comorbid disorders studied was typically associated with a significant increase in

Table 3
Comorbidity of current IED in the context of other current disorders.

Current Comorbid Disorder	NCS-AS Reanalysis OR (95% CI)	NCS-R Reanalysis OR (95% CI)	Clinical Research Analysis OR (95% CI)
Bipolar Disorder	2.29 (1.50–3.51)***	1.71 (0.98–2.99) †	N/A
Depressive Disorder	2.14 (1.64–2.80)***	1.55 (1.07–2.55)*	1.63 (1.20–2.20)**
Non-Phobic Anxiety Disorder	2.23 (1.57–3.17)***	2.39 (1.64–3.50)***	1.34 (0.78–1.66)
Phobic Anxiety Disorder	2.67 (2.19–3.27)***	1.95 (1.40–2.70)***	1.73 (1.15–2.61)**
Substance Use Disorder	2.74 (2.19–3.27)***	2.46 (1.74–3.47)***	N/A
Post-Traumatic Stress Disorder	1.56 (1.06–2.31)*	2.04 (1.29–3.24)*	3.42 (2.09–5.59)***
Bulimia/Binge Eating Disorder	1.05 (0.61–1.82)	1.17 (0.45–3.05)	1.51 (0.63–3.62)

Note: Each column represents the odds ratios from three separate binary logistical regressions adjusted for demographic covariates.
*$p < 0.05$, **$p < 0.01$, ***$p \leq 0.001$, †$p < 0.10$.

Table 4
Mean age of onset (± SD) for lifetime IED with lifetime comorbid syndromal disorders.

NCS-AS Reanalysis			NCS-R Reanalysis		Clinical Research Analysis	
Disorder	IED Age of Onset	Comorbid Dx Age of Onset	IED Age of Onset	Comorbid Dx Age of Onset	IED Age of Onset	Comorbid Dx Age of Onset
Bipolar Disorder	9.6 ± 3.1***	12.1 ± 2.8	14.6 ± 7.1***	21.5 ± 10.8	N/A	N/A
Unipolar Depressive Disorder	10.4 ± 3.2***	11.5 ± 3.1	14.8 ± 7.2***	20.9 ± 11.5	13.9 ± 5.9***	23.6 ± 10.4
Non-Phobic Anxiety Disorder	9.7 ± 3.2	8.8 ± 3.5***	16.2 ± 8.4***	20.0 ± 10.4	14.1 ± 6.1***	21.4 ± 10.6
Phobic Anxiety Disorder	9.8 ± 3.1	6.7 ± 3.0***	13.8 ± 7.3	8.1 ± 5.1***	13.9 ± 6.0	11.5 ± 6.8**
Substance Use Disorder	10.0 ± 3.3***	13.9 ± 1.8	12.3 ± 5.5***	19.5 ± 6.8	14.2 ± 6.8***	20.2 ± 6.2
Post-Traumatic Stress Disorder	10.2 ± 3.5	10.6 ± 4.1	15.4 ± 8.2**	20.2 ± 12.9	13.5 ± 5.9†	15.4 ± 9.0
Bulimia/Binge Eating Disorder	11.0 ± 3.0***	13.3 ± 1.9	13.5 ± 5.2***	17.1 ± 8.2	13.2 ± 6.4***	22.6 ± 9.8

NOTES: *p < 0.05, **p < 0.01, ***p ≤ 0.001, †p < 0.10, by paired *t*-test.

aggression scores of those in the combined group (IED + Comorbid Disorder) compared with either IED alone or the Comorbid Disorder alone. This suggests an interaction between IED and the comorbid disorders examined so that the presence of the two disorders meaningfully increases aggression levels over that seen with either disorder alone. For adolescents (NCS-AS), this was true for all disorders except for PTSD while for adults (NCS-R) this was true for all disorder except for Bulimia/BED. This finding was less apparent for the clinical sample where only adding PTSD to IED was associated with the highest levels of aggression. That said, the clinical sample was not a representative sample of individuals in the community and other factors may have blunted the findings otherwise seen in the two community samples. Overall, these data support the rationale to make an IED diagnosis and the comorbid diagnosis when both are present.

This study has strengths and limitations. First among strengths, these results are based on a reanalysis of two large population-based community data sets and one relatively large clinical research data set. Second, diagnoses were updated to those of DSM-5, though only the A_2 criteria for IED were applied (because questions relevant to the A_1 criteria were not included in the survey instruments used at the time). That said, the clinical research data set assessed IED by both A_1 and A_2 criteria and the results of these analyses rendered very similar results compared with those from the community survey data set. Third, we were able to assess a variable for aggression/impulsivity in all samples and found similar results across the samples.

Limitations include, first, the fact that the community sample data set was collected in the early 2000s and there may have been changes in the community-based epidemiology of IED and the other disorders examined. Unfortunately, we are not aware of another relevant community data set that included raw data referable to IED and these results

Table 5
Composite Aggression Scores as a Function of Adult Disorder Lifetime Comorbidity with Lifetime IED. (ANCOVA: Marginal Means ± SEM) in NCS-AS Reanalysis

Comorbid Disorders (NCS-AS Data) Adolescents	No Dx	Other Dx	Comorbid Disorder	IED	IED + Comorbid Disorder
Bipolar Disorder	- 0.26 ± 0.01	0.19 ± 0.02	0.50 ± 0.04	0.76 ± 0.03	1.12 ± 0.10[a]
Depressive Disorder	- 0.26 ± 0.01	0.15 ± 0.02	0.35 ± 0.03	0.72 ± 0.04	1.02 ± 0.06[a]
All Anxiety Disorder	- 0.26 ± 0.01	0.34 ± 0.03	0.15 ± 0.02	0.76 ± 0.05	0.85 ± 0.05[b,c]
Substance Use Disorder	- 0.26 ± 0.01	0.10 ± 0.02	0.56 ± 0.03	0.64 ± 0.04	1.19 ± 0.06[a,d]
Post-Traumatic Stress Disorder	- 0.26 ± 0.01	0.19 ± 0.02	0.49 ± 0.05	0.73 ± 0.03	1.09 ± 0.1[a]
Bulimia / Binge Eating Disorder	- 0.26 ± 0.01	0.18 ± 0.02	0.45 ± 0.04	0.79 ± 0.03	1.01 ± 0.15[b]
Comorbid Disorders (NCS-R Data) Adults	No Dx	Other Dx	Comorbid Disorder	IED	IED + Comorbid Disorder
Bipolar Disorder	- 0.36 ± 0.02	0.10 ± 0.02	0.72 ± 0.05	0.97 ± 0.05	1.76 ± 0.11[a]
Depressive Disorder	- 0.36 ± 0.02	0.10 ± 0.02	0.22 ± 0.02	0.97 ± 0.06	1.30 ± 0.07[a]
All Anxiety Disorder	- 0.36 ± 0.02	0.06 ± 0.03	0.20 ± 0.02	0.95 ± 0.06	1.19 ± 0.06[a]
Substance Use Disorder	- 0.36 ± 0.02	- 0.00 ± 0.02	0.49 ± 0.03	0.96 ± 0.06	1.34 ± 0.07[a]
Post-Traumatic Stress Disorder	- 0.36 ± 0.02	0.13 ± 0.02	0.32 ± 0.04	1.00 ± 0.05	1.52 ± 0.11[a]
Bulimia / Binge Eating Disorder	- 0.36 ± 0.02	0.14 ± 0.02	0.37 ± 0.06	1.09 ± 0.05	1.34 ± 0.20[b]
Comorbid Disorders (Clinical Research Data) Adults	No Dx	Other Dx	Comorbid Disorder	IED	IED + Comorbid Disorder
Depressive Disorder	- 0.83 ± 0.03	- 0.49 ± 0.04	- 0.30 ± 0.04	0.77 ± 0.04	0.80 ± 0.03[b]
All Anxiety Disorder	- 0.83 ± 0.03	- 0.40 ± 0.03	- 0.40 ± 0.06	0.79 ± 0.03	0.78 ± 0.05[b,c]
Substance Use Disorder	- 0.83 ± 0.03	- 0.44 ± 0.04	- 0.22 ± 0.05	0.75 ± 0.03	0.86 ± 0.04[b]
Post-Traumatic Stress Disorder	- 0.83 ± 0.03	- 0.42 ± 0.03	- 0.17 ± 0.12	0.75 ± 0.03	0.99 ± 0.06[a]
Bulimia / Binge Eating Disorder	- 0.83 ± 0.03	- 0.40 ± 0.03	- 0.12 ± 0.13	0.79 ± 0.03	0.82 ± 0.11[b]

Notes: See text for details on how scores were calculated.
[a] IED + Comorbid Dx > IED > Comorbid Dx > PC > HC.
[b] IED + Comorbid Dx = IED > Comorbid Dx > PC > HC.
[c] Other Dx > Comorbid Dx.
[d] Comorbid Dx = IED.

will have to wait for another DSM-5 targeted community survey to take place. Second, self-reported data is always subject to retrospective bias and the presence or absence of disorders and the timing of onset of disorders could be affected by this factor (Moss and Goldstein, 1979). This is why we limited this analysis to examining current/past year disorders only rather than lifetime disorders. Third, these data do not speak to comorbidity with personality disorders. While personality disorders were not assessed in the NCS-R studies, personality disorder was assessed in the clinical research data set. Findings from that data set have been published (Coccaro et al., 2018) and analyses determined that the presence of any of five personality disorders significantly increased the risk of IED. This included antisocial, borderline, narcissistic, obsessive-compulsive, and paranoid, personality disorders and, as in the present study, aggression scores were highest among those with IED alone and those with IED and any of the "aggressive" personality disorders. While aggression scores among the "aggressive" personality disorders (e.g., antisocial and borderline personality disorder) were higher than those without these personality disorders, the aggression scores were significantly lower among those with an "aggressive" personality disorder who did not meet DSM-5 criteria for IED.

In conclusion, these data suggest that psychiatric comorbidity in IED is similar to that in other, more established, disorders. The observation that the development of IED precedes the onset of most comorbid disorders and the observation that aggression scores displayed by those with IED and a comorbid disorder are often higher than those with IED alone supports the rationale that a diagnosis of both IED and the comorbid disorder should be made when both are present. This should ensure that both sets of disorders are recognized and treated appropriately. This is especially important because only about 20% of those with IED are evaluated or treated for this disorder (Coccaro et al., 2005; Kessler et al., 2006).

Disclosures

Dr. Coccaro reports being on the Scientific Advisory Board of Azevan Pharmaceuticals, Inc. and reports that he is a consultant to Avanir Pharmaceuticals, Inc.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2019.08.012.

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