Research Article

ANXIOUS AND AGGRESSIVE: THE CO-OCCURRENCE OF IED WITH ANXIETY DISORDERS

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Background: *Evidence suggests that impulsive aggression and explosive anger are common among individuals with anxiety disorders; yet, the influence of intermittent explosive disorder (IED) on the onset, course, consequences, and patterns of comorbidity among those with anxiety disorders is unknown.* **Methods:** *Data were drawn from the National Comorbidity Survey Replication (N = 9,282) and Adolescent Supplement (N = 9,632), nationally representative surveys conducted between 2001 and 2004. Diagnoses were based on structured lay-administered interviews. Lifetime diagnoses were assessed with structured instruments. Outcomes included comorbidity, functional and role impairment, and treatment utilization.* **Results:** *Adolescents with a lifetime anxiety disorder had a higher prevalence of a lifetime anger attacks (68.5%) and IED (22.9%) than adolescents without a lifetime anxiety disorder (48.6 and 7.8%, respectively), especially social phobia and panic disorders. Similar elevation was found for adults. Age of onset and course of anxiety disorders did not differ by IED. Severe functional impairment associated with anxiety was higher among adolescents (39.3%) and adults (45.7%) with IED than those without IED (29.2 and 28.2%, respectively). Comorbidity for all other disorders was elevated. However, individuals with anxiety disorders and IED were no more likely to use treatment services than those with anxiety disorders without IED.* **Conclusions:** *Individuals with IED concomitant to anxiety disorder, especially social phobia and panic, are at marked risk for worse functional impairment and a higher burden of comorbidity, but onset and course of anxiety disorder do not differ, and those with anxiety and IED are no more likely to utilize treatment services. Assessment, identification, and specialized treatment of anger in the context of anxiety disorders are critical to reducing burden. Depression and Anxiety 33:101–111, 2016.* © 2015 Wiley Periodicals, Inc.

INTRODUCTION

Aggressive outbursts and anger attacks that are unprovoked or disproportionate to precipitating psychosocial

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stressors affect almost two-thirds of adolescents in the United States.[1] Such outbursts frequently involve physical violence or property destruction and contribute to widespread societal and individual harm,[2,3] but may involve verbal aggression as well, and usually have out-of-proportion anger as a core feature. When such outbursts are recurrent, a diagnosis of intermittent explosive disorder (IED) is often indicated.[2] IED is relatively common, with DSM-IV lifetime prevalence estimates between 7 and 8% among adolescents and adults in the US general population.[1,4] Despite the high prevalence, early age of onset,[5] high personal and societal costs,[4] low uptake of treatment services among individuals with IED,[1,4] and serious consequences associated with aggressive outbursts and IED, little research attention has been devoted to understand this disorder. Emerging evidence indicates that IED is best described as part of an externalizing dimension of disorders such as conduct and substance use disorders, but is also associated with internalizing disorders such as depression and anxiety.[6] Particular associations with specific types of internalizing disorders and the implications of IED comorbidity for management of internalizing disorders remain inadequately understood.

Although anxiety disorders are typically characterized by social withdrawal, inhibition and shyness, and discomfort in social expression, individuals with anxiety disorders often express intense and out-of-proportion anger and aggression.[7,8] Emerging evidence indicates that meaningful subgroups of individuals with social phobia exhibit symptoms involving violent behavior, aggression, and novelty seeking.[9] Individuals with anxiety disorders frequently perceive criticism or rejection from others,[10,11] engage in self-criticism, and have difficulty discussing negative emotional states with others. Because suppression of negative emotions has the counterproductive effect of heightening physiological arousal,[12] such suppression might contribute to intense anger expression and aggressive outbursts over time. Indeed, evidence from clinical samples indicates heightened anger and aggression among individuals with anxiety disorders,[9] high co-occurrence of anxiety disorders with antisocial behavior and aggression,[13] and poor treatment outcomes for individuals with anxiety who have co-occurring anger problems.[9]

However, little is known about patterns of co-occurrence across different anxiety disorders or the impact of aggressive outbursts on the course and severity of anxiety over the life course. Difficulty in controlling aggression and anger is likely associated with a host of negative consequences for individuals with anxiety disorders (e.g., greater fear and avoidance of situations that previously triggered aggression), although little research has examined this possibility. Individuals with IED have deficits in general emotion regulation, not just anger and aggression, suggesting that broader comorbidities should also be considered.[14] In particular, there is a lack of research on how aggression and IED influence anxiety disorders in adolescence, despite the fact that

uncontrollable aggression and the use of aggression as a proactive emotion regulation strategy are more common among adolescents than adults,[15] and IED typically begins in early adolescence.[1,4]

The present study utilizes data from the National Comorbidity Survey Replication (NCS-R) and the associated Adolescent Supplement (NCS-A) to examine the prevalence and consequences of aggressive outbursts and IED among adolescents and adults with anxiety disorders and the association of IED with course, severity, and treatment utilization for anxiety. We focus on social phobia, specific phobia, panic disorder, and generalized anxiety disorder (GAD) as these disorders are common anxiety disorders and have been previously identified in clinical research as the most commonly co-occurring with aggressive outbursts and anger attacks.[8,9,16]

METHODS

STUDY DESIGN

NCS-R. The NCS-R was a nationally representative multistage clustered-area probability sample of adults aged 18+ in the United States, with a 70.9% response rate ($N = 9,282$).[17] Structured interviews including IED diagnostic items were administered to a subsample of respondents ($n = 5,692$) including those who met lifetime criteria for a mental disorder in the larger sample and a probability sample of those who did not. Sample weights were generated to account for selection probabilities and nonparticipation as well as weight to the 2000 census. Greater details of the design and procedures can be found elsewhere.[17]

NCS-A. The NCS-A involved a nationally representative dual-frame household and school sample of adolescents aged 13–18 and their parents, collected in 2001–2004.[18,19] The total sample size was 10,148, and included a household and school sample. The household sample included adolescents whose parents participated in NCS-R ($n = 904$; 86.8% response rate). The school sample was drawn from a representative sample of schools in the NCS-R counties ($n = 9,244$, 82.6% response rate). The initial response rate of schools was low (28%). Schools that declined participation were replaced with demographically matched schools.[19] One parent or guardian completed a self-administered questionnaire (SAQ; response rate, conditional on adolescent participant, was 82.5% in the household sample and 83.7% in the school sample). Because of exclusion criteria (see below), the final analytic sample included 9,632 respondents.

Parents provided written informed consent before the adolescent was approached, and subsequent written consent was obtained from the adolescent. Sample weights accounted for variation in within-household probability of selection in the household sample and residual discrepancies between sample and population sociodemographic and geographic distributions.[18] For both data sources, institutional review boards of Harvard Medical School and University of Michigan approved study procedures, and the institutional review board of Columbia University approved the present analyses.

Measures

Respondents in both NCS-R and NCS-A were interviewed with the Composite International Diagnostic Interview (CIDI), a fully structured lay-administered interview.[20–22]

Anger Attacks and IED. The development of criteria that define and distinguish IED remains an active area of research.[23,24] In this report, we used DSM-IV criteria[25] as operationalized in the CIDI. DSM-IV criterion A assessed attacks that were "out-of-control,"

operationalized by requiring the respondent to report at least one of three types of anger attacks: (1) "when all of a sudden you lost control and broke or smashed something worth more than a few dollars," (2) "when all of a sudden you lost control and hit or tried to hurt someone," and (3) "when all of a sudden you lost control and threatened to hit or hurt someone." DSM-IV criterion B assessed attacks that were "out-of-proportion," operationalized by requiring the respondent to report that he or she "got a lot more angry than most people would have been in the same situation," that the attacks occurred "without good reason," or that the attacks occurred "in situations where most people would not have had an anger attack." Thus, attacks could be out-of-control, out-of-proportion, both, or neither. We assess all four options in the present manuscript. Respondents were also queried regarding whether symptoms were not better accounted for by substance use, a medical condition, or another psychiatric disorder, and such respondents were precluded from diagnosis. Those respondent with ≥3 such attacks in their lifetime were considered to have IED. We use the term "anger attacks" to describe this phenomenon in keeping with prior literature on these data,[1,4] and because they are described as "anger attacks" in the instrument, but note that both anger and aggression are assessed in this instrument and that aggressive impulses, independent of anger, are central to the clinical and diagnostic assessment of such outbursts. We also excluded individuals with manic episodes, hypomanic episodes, or bipolar I or II disorder, given concerns about diagnostic overlap.[26] Although diagnoses in both NCS-R and NCS-A were validated using a clinical reappraisal of nested probability samples, IED was not included in the clinical reappraisal interview schedule.

Anxiety Disorders. Anxiety disorders were diagnosed using DSM-IV criteria, based on lifetime experiences. Four anxiety disorders were included in the current study: social phobia, specific phobia, GAD, and panic disorder. In the NCS-R, blinded clinical reappraisals using the Structured Clinical Interview (SCID) for DSM-IV[27] in a nested probability subsample of participants established good concordance of anxiety disorders diagnosed in the CIDI and the SCID.[22] In the NCS-A, respondents were positive for an anxiety disorder if meeting criteria either by the CIDI or the SAQ. A blinded clinical reappraisal sample was assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Lifetime Version (K-SADS[28]; high concordance rates between the CIDI/SAQ diagnoses and K-SADS were observed for all anxiety diagnoses).[21]

Other Psychiatric Disorders. The CIDI operationalizes DSM-IV criteria for a broad range of other Axis I disorders. The present study examined comorbidity of anxiety disorders with the following disorders: mood disorders (dysthymia, major depressive episodes, major depressive disorder), substance disorders (alcohol abuse, alcohol dependence, drug abuse, drug dependence, nicotine dependence), and a combined category of other disorders (anorexia nervosa, attention deficit hyperactivity disorder [ADHD], binge eating disorder, bulimia nervosa, conduct disorder [CD], and oppositional defiant disorder [ODD]). In the NCS-A, parents provided information in the SAQ regarding the child's symptoms of major depression/dysthymia, ADHD, ODD, and CD, based on previous research indicating that parents' assessments of behavior are informative for these diagnoses.[29,30] All DSM-IV hierarchy and exclusion rules were applied. Reliability and validity of these diagnoses is similar to other large-scale surveys of psychiatric disorders and has been firmly established in previous research.[21,22]

Functional Impairment and Disability. Among those with an anxiety disorder, respondents were asked how many days in the past year they could not attend work, school, or other duties that were required of them due to the symptoms of their anxiety disorder. All respondents with a mental health diagnoses were assessed with the Sheehan Disability Scales[31] measuring the extent to which mental health symptoms interfered in the following domains: home life, school or work, family relationships, and social life. Response options were none (0), mild (1–3), moderate (4–6), severe (7–9), and very severe (10). Consistent with prior research,[1,4] severe impairment was operationalized as a score of 7 or higher.

Treatment Utilization. For each focal disorder assessed in the CIDI, respondents were asked whether they had ever received professional treatment.

Sociodemographics Characteristics. Race (non-Hispanic White, non-Hispanic Black, Native American/Alaska Native, Asian/Pacific Islander, Hispanic) and sex were included as demographic control variables in both NCS-R analyses and NCS-A analyses. In the NCS-R, age was categorized as 18–29, 30–44, 45–59, and 60+. In the NCS-A, each age was designated as a category (six-level categorical variable with levels from 13 to 18). Highest completed education completed by the respondent (NCS-R) or the parent (NCS-A) was also included (less than high school, high school, some college, or college or higher).

STATISTICAL ANALYSIS

In both the NCS-R and NCS-A, lifetime prevalence of anger attacks and IED, disability, comorbidity, and treatment utilization were estimated using cross-tabulation and chi-square tests comparing those with a lifetime diagnosis of any of the four focal anxiety disorders (social phobia, specific phobia, GAD, or panic disorder) to those without these disorders, and then comparing those with each disorder specifically to those with no anxiety disorders. Differences in mean number of attacks, years with disorder, and days out of role were examined using t-tests, as was age of onset of IED. In all analyses, adjusted analyses used logistic regression for dichotomous outcomes and linear regression for continuous outcomes. Differences in age of onset of anxiety disorders were tested using t-tests for mean differences as well as Kaplan–Meier survival curves and log-rank nonparametric tests. Analyses were conducted in SAS version 9.3 and SAS-callable SUDAAN. Complex survey weights and sampling weights were used to adjust estimates and standard errors for the complex sampling design of both studies. Regression models were adjusted for age, race/ethnicity, education, and sex.

RESULTS

PREVALENCE OF ANGER ATTACKS AND IED

The prevalence of anger attacks and IED among those with any anxiety disorder and each specific anxiety disorder is shown in Table 1, for both the NCS-A and NCS-R. Adolescents with a lifetime anxiety disorder had a higher prevalence of total anger attacks, were more likely to have 3+ lifetime anger attacks that were out-of-proportion to the stressor, including both those out-of-control (22.9 vs. 8.0%) and not out-of-control (13.1 vs. 10.6%), and had a higher lifetime prevalence of IED (22.9%) than adolescents without a lifetime anxiety disorder (7.8%). These results were consistent across anxiety diagnoses: total anger attacks, repeated attacks that were out-of-proportion and out-of-control, and lifetime IED were each more common among adolescents with lifetime social phobia, GAD, specific phobia, and panic disorder than among adolescents with no anxiety diagnosis. These results were mirrored in the NCS-R adult data. Although the overall prevalence of anger attacks and IED was generally lower among adults than

TABLE 1. Distribution of lifetime anger attacks and IED among individuals with lifetime anxiety disorders

	Any lifetime anxiety disorder		Lifetime social phobia		Lifetime GAD		Lifetime specific phobia		Lifetime panic disorder		Control: No lifetime anxiety disorder	
	Prevalence (%; SE)	Mean (SE) no. of attacks	Prevalence (%; SE)	Mean (SE) no. of attacks	Prevalence (%, SE)	Mean (SE) no. of attacks	Prevalence (%, SE)	Mean (SE) no. of attacks	Prevalence (%, SE)	Mean (SE) no. of attacks	Prevalence (%, SE)	Mean (SE) no. of attacks
NCS-A												
1–2 attacks	25.1 (1.8)	1.6 (0.0)	25.6 (2.4)	1.7 (0.0)*	14.4 (3.0)	1.5 (0.0)	27.2 (1.8)*	1.6 (0.0)	23.7 (3.8)	1.5 (0.1)	22.7 (0.8)	1.5 (0.0)
≥3 not out-of-proportion attacks	7.5 (0.9)	1.36 (1.4)	6.4 (1.0)	11.4 (2.5)	9.0 (3.2)	11.1 (0.0)	7.1 (0.9)	8.0 (0.7)	10.2 (3.4)	6.1 (0.5)	7.4 (0.4)	11.0 (2.4)
≥3 out-of-proportion, not out-of-control attacks	13.1 (1.1)*	23.0 (7.5)	14.2 (1.2)*	32.8 (13.1)	15.1 (2.3)	8.1 (0.3)	12.4 (1.1)	17.4 (5.6)	14.6 (4.0)	20.5 (0.5)	10.6 (0.6)	15.4 (3.4)
≥3 out-of-proportion, out-of-control attacks	22.9 (1.4)*	25.5 (4.1)	22.7 (1.5)*	19.9 (4.3)	26.1 (3.5)*	33.9 (4.8)	22.9 (2.0)*	24.5 (4.9)	33.3 (4.7)*	31.1 (6.4)	8.0 (0.6)	22.4 (4.2)
Total prevalence of attacks	68.5 (1.7)*	14.6 (2.1)*	68.9 (2.5)*	15.0 (3.4)	64.6 (3.3)*	17.5 (2.3)	69.5 (1.9)*	12.6 (2.0)	81.7 (3.3)*	17.5 (3.4)	48.6 (1.0)	9.4 (1.1)
IED	22.9 (1.4)*	25.2 (4.1)	23.2 (1.6)*	19.3 (4.1)	26.7 (3.6)*	33.0 (4.6)	22.6 (1.9)*	24.5 (5.0)	33.8 (4.8)*	30.5 (6.2)	7.8 (0.6)	21.3 (4.1)
Age of IED onset	10.0 (0.1)		10.3 (0.2)		9.0* (0.6)		10.1 (0.2)		10.0 (0.5)		10.0 (0.1)	
NCS-R												
1-2 attacks	19.9 (1.1)*	1.5 (0.0)	21.5 (1.7)*	1.5 (0.0)	19.4 (2.5)*	1.5 (0.1)	20.4 (1.4)*	1.6 (0.0)	18.2 (1.8)*	1.7 (0.1)	14.5 (0.5)	1.5 (0.0)
≥3 not out-of-proportion attacks	9.3 (1.0)	14.4 (6.1)	8.9 (0.8)	23.9 (12.3)	9.8 (2.4)	6.8 (0.3)	7.2 (1.1)	21.6 (15.5)	13.5 (1.8)*	27.1 (22.8)	7.6 (0.4)	11.0 (2.3)
≥3 out-of-proportion, not out-of-control attacks	11.1 (0.8)*	20.2 (3.2)	10.5 (1.0)*	19.3 (1.8)	11.0 (1.6)*	11.1 (0.6)	11.7 (1.4)*	26.1 (3.2)	10.1 (1.9)*	12.2 (3.8)	5.1 (0.3)	17.7 (6.6)
≥3 out-of-proportion, out-of-control attacks	15.1 (0.7)*	24.8 (3.0)	19.3 (1.4)*	27.7 (4.0)	16.5 (1.9)*	25.3 (6.2)	15.4 (1.2)*	21.0 (3.0)	16.7 (2.0)*	21.5 (4.0)	3.5 (0.3)	30.5 (6.2)
Total prevalence of attacks	55.3 (1.3)*	13.8 (1.7)	60.2 (1.7)*	16.3 (3.5)	56.8 (3.0)*	11.2 (2.0)	54.6 (2.4)*	14.9 (2.4)	58.2 (2.4)*	15.0 (5.6)	30.7 (0.8)	9.8 (1.5)
IED	13.5 (0.8)*	24.2 (3.4)	16.3 (1.2)*	29.0 (4.7)	15.6 (1.9)*	25.2 (6.6)	13.6 (1.2)*	18.3 (2.0)	16.4 (2.0)*	17.5 (2.8)	3.3 (0.3)	31.4 (6.8)
Age of IED onset	14.4 (0.5)		14.4 (0.6)		14.7 (1.0)		13.8 (0.6)		15.1 (0.9)		14.1 (0.4)	

*Significant differences between column anxiety disorder and control ($P < .05$).

adolescents, those with social phobia, GAD, specific phobia, and panic disorder were more likely to have recurrent anger attacks that were out-of-proportion and out-of-control, as well as lifetime IED (13.5–16.4%), than adults without a lifetime anxiety disorder (3.3%).

Age of onset of IED was younger among those with a lifetime diagnosis of GAD compared to those without in the NCS-A data (9.0 vs. 10.1, $P = .03$); no other age of onset differences emerged comparing those with and without specific anxiety disorders, in either adolescents or adults. Overall (data not shown), Kaplan–Meier curves for age of onset showed no significant differences; IED has a younger mean age of onset than all anxiety disorders, safe for specific phobia with a mean age of onset of 9.3 in adults and 6.1 in adolescents, indicating that with the exception of specific phobia, IED most often precedes the development of anxiety disorders.

IED AND ANXIETY DISORDER COURSE

We examined whether the course of anxiety disorders differed among those with and without IED. Among adults with lifetime GAD, those without IED had an average of 0.43 years shorter duration of GAD compared to those with IED (95% CI–0.63, –0.23). There were no other differences in anxiety disorder course among either adolescents or adults. Kaplan–Meier curves indicated that no differences in average age of anxiety disorder onset were observed as a function of lifetime IED among adolescents or adults (results available upon request).

IED AND ANXIETY DISORDER IMPAIRMENT

Table 2 displays severity of functional impairment among those with lifetime anxiety disorders with and without lifetime IED. Adolescents with IED had more days out of role associated with their anxiety disorder ($\beta = -0.76$, 95% CI–1.12, –0.41), and greater impairment in work (24.4%) and interpersonal (18.1%) domains than those without IED (14.7 and 11.5%, respectively). Adults with IED had greater impairment in home (16.0%), interpersonal (26.5%), and social (32.4%) domains than those without IED (11.8, 16, and 19.2%, respectively). Overall, 39.3% of adolescents and 45.7% of adults with a lifetime anxiety disorder and IED had severe disability in at least one domain, compared with 29.2 and 28.2%, respectively, of those without IED.

IED AND ANXIETY DISORDER COMORBIDITY

Both adolescents and adults with lifetime anxiety disorders and IED, compared to those without IED, had increased odds of meeting criteria for another lifetime psychiatric disorder (Table 3, Supporting Information Tables S1 and S2). Adolescents with an anxiety disorder and IED were more likely to have additional lifetime mood (OR = 1.96, 95% CI 1.46–2.64), substance use (OR = 3.30, 95% CI 2.30–4.71), and impulse control (OR = 1.95, 95% CI 1.33–2.84) disorders. Adults with

any anxiety disorder and IED were also more likely to also have additional lifetime mood (OR = 1.59, 95% CI 1.10–2.28), anxiety (OR = 1.79, 95% CI 1.08–2.97), substance use (OR = 1.68, 95% CI 1.21–2.34), and impulse control (OR = 1.76, 95% CI 1.21–2.58) disorders than those without IED. When anxiety disorders were examined separately, the highest rates of comorbidity were observed among individuals with social or specific phobia and with IED (see Table 3).

In Supporting Information Tables S1 and S2, we provide unadjusted prevalence estimates of comorbidity between IED and other disorders among those with each anxiety disorder, among adolescents and adults, respectively, and in Supporting Information Tables S3 and S4, we provide adjusted ORs for these comparisons for adolescents and adults, respectively.

IED AND ANXIETY DISORDER TREATMENT UTILIZATION

Finally, we examined treatment utilization for anxiety disorders among those with an anxiety disorder with and without lifetime IED. Table 4 shows the proportion of individuals with a diagnosis who utilized treatment services. Treatment utilization for anxiety disorders was low, and there were few differences in treatment utilization when IED was present, among either adolescents or adults. In adjusted analyses among adults (Supporting Information Table S5), individuals with lifetime panic disorder and IED were significantly less likely to utilize anxiety disorder treatment (OR = 0.55, 95% CI 0.30, 1.00) and panic disorder treatment (OR = 0.47, 95% CI 0.23, 0.93) than those without IED. No other significant differences emerged.

DISCUSSION

Based on analysis of national population based data, we document four central patterns that are consistent in both adolescents and adults. First, individuals with anxiety disorders experience more anger attacks (which are defined at their core by both anger and aggression in this instrument), including those that are out-of-control and out-of-proportion to precipitating circumstances, and are more than three times as likely to meet criteria for lifetime IED than those without an anxiety disorder. A total of 56% of adults and 69% of adolescents with an anxiety disorder experienced a lifetime anger attack, compared with 31 and 49% of those without an anxiety disorder, respectfully. Second, individuals with an anxiety disorder and comorbid IED had higher levels of functional impairment associated with their anxiety than those without comorbid IED and increased risk of a broad range of comorbid disorders including mood, substance use, and behavior disorders. Elevated comorbidity associated with IED was particularly prominent among individuals with social and specific phobias. Age of IED onset is young, approximately age 10 in the adolescent sample and age 14 in the adult sample; IED

TABLE 2. Impairment associated with anxiety disorders among those with and without comorbid IED in the United States

	Any lifetime anxiety disorder		Lifetime social phobia		Lifetime GAD		Lifetime specific phobia		Lifetime panic disorder	
	With lifetime IED	Without lifetime IED	with lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED
NCS-A										
12-month prevalence among lifetime cases (%; SE)	91.5 (2.2)	89.6 (2.1)	95.2 (2.5)	93.1 (2.9)	74.9 (8.9)	84.5 (6.3)	89.7 (3.0)	86.0 (3.0)	95.2 (4.3)	82.2 (10.3)
Days out of role associated with anxiety disorder, beta comparing without vs. with IED (95% CI)	−0.76 (−1.12, −0.41)		−0.70 (−1.47, 0.07)		−0.36 (−1.26, 0.55)		−0.83 (−1.40, −0.26)*		−0.17 (−1.46, 1.11)	
Severe impairment on Sheehan Disability Scales[a], (%, SE) Home	4.6 (1.8)	5.2 (1.6)	2.5 (2.3)	3.3 (2.2)	4.0 (4.3)	5.6 (5.5)	3.4 (1.4)	3.6 (1.3)	6.7 (5.7)	8.2 (5.2)
Work	24.4 (4.3)*	14.2 (2.4)*	27.3 (7.5)*	14.5 (3.7)*	33.6 (18.0)	32.3 (12.4)	11.5 (4.2)	8.2 (2.6)	17.0 (11.3)	14.9 (7.6)
Interpersnl	18.1 (3.9)*	11.0 (2.2)*	10.7 (4.6)	9.2 (3.6)	66.0 (16.9)*	30.2 (12.1)*	15.3 (5.1)*	8.4 (2.6)*	9.6 (5.8)	9.4 (5.3)
Social	19.4 (3.5)	17.7 (2.5)	23.6 (5.9)	21.6 (4.8)	41.4 (14.7)	32.6 (10.1)	12.3 (4.5)	8.0 (2.6)	21.6 (12.0)	21.8 (9.9)
Summary	39.3 (4.1)*	28.5 (2.8)*	42.0 (7.1)	35.5 (5.3)	85.2 (12.2)	58.6 (12.7)	29.4 (5.8)*	15.9 (3.2)*	31.2 (13.2)	29.7 (10.6)
NCS-R										
12-month prevalence among lifetime cases (%; SE)	73.8 (3.8)	67.6 (2.5)	63.7 (5.9)	58.5 (4.0)	62.1 (8.0)	59.9 (5.2)	75.0 (4.8)	73.3 (3.7)	65.1 (9.2)	58.1 (6.0)
Days out of role associated with anxiety disorder, beta comparing without versus with IED (95% CI)	0.01 (−0.49, 0.50)		0.09 (−0.97, 1.15)		0.65 (0.08, 1.21)*		0.44 (−0.51, 1.39)		−0.06 (−0.84, 0.72)	
Severe impairment on Sheehan Disability Scales[a], (%, SE) Home	16.0 (3.7)*	11.0 (2.1)*	8.0 (3.6)	7.6 (2.2)	22.4 (10.0)	18.4 (6.4)	6.7 (3.3)	6.2 (2.2)	26.8 (10.5)	19.1 (6.3)
Work	19.4 (4.7)	12.8 (2.0)	15.6 (5.2)	13.3 (3.1)	22.5 (11.3)	18.8 (6.8)	6.9 (3.5)	7.5 (2.2)	21.5 (10.4)	21.3 (6.8)
Interpersonl	26.5 (4.8)*	15.8 (2.2)*	20.8 (6.1)	21.1 (4.3)	34.4 (9.6)	24.9 (6.8)	10.9 (4.9)	6.0 (2.2)	12.2 (6.6)	19.6 (7.2)
Social	32.4 (4.8)*	18.9 (2.5)*	29.2 (6.6)	26.0 (4.3)	49.5 (13.4)	32.6 (8.5)	14.5 (5.7)	8.2 (2.6)	25.3 (10.9)	23.5 (7.0)
Summary	45.7 (4.9)*	28.0 (2.9)*	38.2 (7.2)	32.1 (4.9)	67.9 (11.1)	46.6 (8.7)	23.6 (6.8)	14.6 (3.1)	44.7 (12.9)	37.5 (7.8)

All models were adjusted for age, race, education, and sex.

[a]Severe impairment defined as scoring a 7 or higher on the Sheehan Disability Scales.

*Significant differences in impairment between anxiety disorder with IED and anxiety disorder without IED (P < .05).

TABLE 3. Prevalence and odds ratio for the association between IED and psychiatric disorders among those with anxiety disorders in the United States

	Any lifetime anxiety disorder		Lifetime social phobia		Lifetime GAD		Lifetime specific phobia		Lifetime panic disorder	
	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED
NCS-A										
Mood disorders	30.9 (2.7)*	18.7 (1.4)*	32.8 (3.7)*	23.3 (2.2)*	52.3 (7.8)*	33.4 (6.0)*	31.7 (3.7)*	17.9 (1.7)*	43.4 (8.9)	30.7 (7.4)
	1.96 (1.46, 2.64)		1.64 (1.10, 2.44)		1.60 (0.80, 3.21)		2.18 (1.43, 3.32)		1.68 (0.63, 4.50)	
Anxiety disorders	87.6 (2.3)	82.0 (1.5)	74.3 (4.1)*	62.3 (2.3)*	75.7 (4.7)	82.1 (3.0)	72.2 (3.4)*	58.4 (1.9)*	100.0 (0.0)	100.0 (0.0)
	1.58 (0.97, 2.57)		1.77 (1.07, 2.91)		1.13 (0.50, 2.59)		1.89 (1.23, 2.88)		1.0 (0)	
Substance use disorders	33.0 (3.8)*	13.4 (1.7)*	36.3 (5.1)*	16.1 (2.7)*	29.1 (9.7)*	11.8 (1.9)*	33.6 (4.0)*	12.4 (1.5)*	29.8 (6.1)	27.6 (7.3)
	3.30 (2.30, 4.71)		3.10 (1.91, 5.03)		1.96 (0.94, 4.10)		3.47 (2.56, 4.71)		1.06 (0.38, 2.94)	
Other disorders[a]	24.6 (2.9)*	14.2 (1.4)*	25.5 (3.8)	17.5 (2.1)	17.0 (5.8)	13.1 (2.9)	28.5 (4.0)*	14.2 (1.2)*	24.6 (7.3)	21.2 (5.3)
	1.95 (1.33, 2.84)		1.58 (0.92, 2.71)		2.10 (0.75, 5.87)		2.28 (1.43, 3.61)		1.17 (0.48, 2.84)	
NCS-R										
Mood disorders	48.4 (4.1)*	37.4 (1.6)*	52.3 (5.3)	42.4 (2.0)	57.8 (7.7)	52.8 (3.7)	44.0 (5.0)	36.9 (1.6)	53.9 (5.1)	43.4 (4.0)
	1.59 (1.10, 2.28)		1.49 (0.94, 2.38)		1.14 (0.62, 2.12)		1.34 (0.86, 2.07)		1.67 (0.88, 3.16)	
Anxiety disorders	91.2 (1.8)*	85.9 (1.1)*	84.8 (2.9)*	69.5 (2.0)*	88.7 (3.4)	79.4 (2.3)	90.7 (2.4)*	72.5 (1.5)*	100.0 (0.0)	100.0 (0.0)
	1.79 (1.08, 2.97)		2.46 (1.49, 4.06)		1.94 (0.93, 4.06)		3.72 (1.90, 7.28)		1.0 (0)	
Substance use disorders	43.8 (3.9)*	28.3 (1.6)*	47.8 (5.1)*	30.2 (1.8)*	45.0 (7.1)	32.1 (3.6)	43.2 (4.1)*	28.3 (2.3)*	49.0 (6.7)*	29.9 (2.8)*
	1.68 (1.21, 2.34)		1.81 (1.26, 2.60)		1.47 (0.74, 2.91)		1.60 (1.04, 2.46)		1.86 (1.05, 3.29)	
Other disorders[a]	33.7 (2.9)*	17.8 (1.1)*	39.9 (4.9)*	21.2 (1.7)*	23.4 (5.2)	18.7 (2.5)	34.9 (4.2)*	17.4 (1.5)*	22.9 (5.9)	17.2 (2.3)
	1.76 (1.21, 2.58)		2.17 (1.26, 3.73)		1.10 (0.56, 2.15)		1.96 (1.16, 3.31)		0.91 (0.45, 1.83)	

All odds ratios were adjusted for age, race, education, and sex.

[a]Anorexia nervosa, attention deficit hyperactivity disorder (ADHD), binge eating disorder, bulimia nervosa, conduct disorder (CD), and oppositional defiant disorder (ODD).

*Significant differences in comorbidity between anxiety disorder with IED and anxiety disorder without IED ($P < .05$).

TABLE 4. Prevalence of 12-month treatment of anxiety disorders among those with and without comorbid IED

	Any lifetime anxiety disorder		Lifetime social phobia		Lifetime GAD		Lifetime specific phobia		Lifetime panic disorder	
	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED	With lifetime IED	Without lifetime IED
NCS-A										
(%, SE) Any separation anxiety treatment	0.4 (0.3)	0.5 (0.2)	0.5 (0.5)	1.0 (0.5)	0.0 (0.0)*	0.2 (0.2)*	0.3 (0.3)	0.6 (0.4)	0.0 (0.0)*	5.3 (3.7)*
Any agoraphobia treatment	1.8 (0.8)	0.9 (0.3)	2.0 (0.9)	1.2 (0.6)	0.3 (0.3)	1.8 (1.1)	2.1 (1.2)	0.8 (0.4)	6.1 (3.2)	7.8 (4.3)
Any GAD treatment	4.7 (1.9)	2.8 (0.6)	3.0 (1.5)	4.3 (1.2)	21.7 (4.2)*	12.6 (2.7)*	4.2 (2.1)	2.3 (0.7)	4.6 (2.9)	13.0 (4.8)
Any panic disorder treatment	3.6 (1.3)	2.4 (0.5)	2.0 (0.9)	3.0 (1.0)	0.0 (0.0)*	3.2 (1.9)*	3.7 (2.0)	1.8 (0.5)	19.9 (4.2)	16.4 (3.5)
Any PTSD treatment	2.1 (0.8)	1.2 (0.4)	2.3 (1.3)	2.0 (0.8)	1.4 (1.3)	2.3 (1.8)	2.1 (1.1)	1.4 (0.6)	5.4 (3.8)	4.4 (3.4)
Any social phobia treatment	2.5 (1.0)	2.8 (0.6)	5.3 (1.9)	5.6 (1.2)	2.5 (2.1)	6.9 (2.3)	2.4 (1.1)	2.5 (0.8)	7.3 (3.2)	7.0 (4.4)
Any specific phobia treatment	2.2 (1.0)	1.6 (0.4)	1.1 (0.5)	2.2 (0.7)	0.0 (0.0)*	2.2 (1.4)*	3.5 (1.6)	2.3 (0.5)	5.0 (2.5)	2.7 (1.3)
Any treatment (any of the above)	11.0 (2.2)	6.7 (0.9)	8.1 (2.3)	10.2 (1.8)	21.7 (4.2)	13.4 (2.4)	9.7 (2.6)	6.2 (1.1)	27.3 (5.3)	21.8 (5.0)
NCS-R										
(%, SE) Any separation anxiety treatment	0.9 (0.6)	1.5 (0.3)	1.6 (1.0)	2.0 (0.6)	2.7 (1.9)	2.0 (0.7)	1.4 (1.1)	1.1 (0.4)	2.2 (2.3)	2.1 (0.8)
Any agoraphobia treatment	4.4 (1.6)	3.8 (0.4)	6.7 (2.5)	6.1 (0.8)	8.2 (4.6)	4.1 (1.0)	3.3 (1.8)	4.4 (0.9)	6.8 (3.4)	11.1 (1.9)
Any GAD treatment	10.5 (1.8)	10.8 (0.9)	9.2 (2.7)	11.9 (1.1)	24.5 (5.9)	23.0 (1.9)	9.2 (2.4)	10.1 (1.4)	11.7 (3.8)	21.0 (2.9)
Any panic disorder treatment	7.1 (2.2)	7.4 (0.6)	6.7 (2.4)	8.0 (0.8)	8.5 (4.3)	7.0 (1.3)	6.2 (1.5)	7.5 (1.0)	15.4 (4.5)*	30.3 (2.5)*
Any PTSD treatment	3.1 (1.0)	2.7 (0.5)	5.0 (1.6)	3.3 (0.5)	3.3 (2.0)	4.6 (1.1)	0.4 (0.5)	2.5 (0.6)	2.5 (2.6)	5.8 (1.6)
Any social phobia treatment	6.4 (1.4)	5.6 (0.6)	10.6 (2.4)	11.2 (1.1)	7.2 (4.5)	5.6 (1.0)	4.9 (2.0)	5.0 (0.9)	6.8 (3.0)	10.1 (1.3)
Any specific phobia treatment	1.7 (0.7)	3.6 (0.5)	2.3 (1.1)	3.8 (0.7)	2.2 (1.6)	3.0 (0.7)	3.3 (1.4)	6.7 (1.0)	3.2 (1.7)	6.1 (1.4)
Any treatment (any of the above)	17.5 (2.1)	17.7 (0.9)	16.6 (2.6)	19.9 (1.3)	27.5 (5.2)	25.6 (2.0)	13.8 (2.0)	17.3 (1.5)	22.0 (5.4)*	36.8 (3.1)*

*Significant differences in comorbidity between anxiety disorder with IED and anxiety disorder without IED (*P* < .05).

onset thus precedes the onset of most other disorders based on available evidence, safe for specific phobias. Third, despite poorer functioning and greater comorbidity, individuals with comorbid anxiety disorders and IED were no more likely to utilize treatment services for their anxiety; indeed, individuals with panic disorder and IED were significantly less likely to use treatment services than those without IED. Finally, there were no meaningful differences in age of onset or course of anxiety disorders as a function of IED, suggesting that although IED might increase severity of impairment and risk of comorbidity psychiatric disorders for those with anxiety disorders, it does not influence disorder persistence.

These findings suggest that impulsive anger and aggression leading to physical violence, property destruction, and threats of violence is common among adolescents and adults with anxiety disorders, and suggest that clinicians query potential anger and aggression issues when assessing new patients with anxiety problems. These findings highlight the clinical importance of assessing aggression anger responses, including anger attacks and IED, among individuals with anxiety disorders including social and specific phobias, panic disorder, and GAD. Anxiety researchers and clinicians should be aware that a subtype of anxious individuals with heightened anger expression is common in the general population.[9, 16, 32]

For those with anxiety disorders, anger and aggression may be a means to avoid feared stimuli; an anxious individual may express extreme or out-of-proportion anger in order to disengage with the stimulus.[33] Further, anxiety-disordered individuals may have difficulty in expressing negative emotional states, which may lead to heightened physiological arousal[12] that can result in intense displays of anger and aggression.[34] Alternatively, children who are aggressive or angry may be at higher risk of developing anxiety disorders, potentially due to isolation from peers as a result of aggressive behavior, physiological hyperarousal, fear of losing control of their anger, or other pathways. Because of the young age of onset of IED, children and adolescents who exhibit anger problems at a young age should be considered at particular risk for development of comorbidity and other mental health problems.

The mechanisms that underlie these associations warrant further study. Commonalities between IED and anxiety disorders include a diminished ability to regulate emotions and tolerate distress and heightened psychological arousal.[24, 35] Fettich et al. document that individuals with IED demonstrate global emotional regulation deficits, beyond anger alone.[14] Both IED[36] and anxiety disorders[37] are familial, suggesting there may be at least some degree of genetic vulnerability to both. Emerging evidence also indicates that inflammatory processes may underlie the association between anger and psychiatric disorders.[38] Further, evidence indicates that both anxiety and anger attacks involve similar neurobiological pathways with decreased inhibitory control

over limbic structures like the amygdala by the prefrontal cortex.[39–41] Anxiety, anger, and aggression may arise from common processes involving fear circuitry,[42] though limited literature is available at present to fully evaluate such pathways. Regardless of the mechanism, individuals experiencing both intense and out-of-control anger expression and anxiety disorders may require a more intensive and specialized program of treatment involving the development of effective emotion regulation and interpersonal skills.[43]

Of particular concern, adolescents with comorbid anxiety disorders, particularly social phobia, and IED have high rates of alcohol and drug dependence. Previous studies have demonstrated that impulse control disorders such as IED are highly comorbid with substance use disorders,[44] and the presence of at least one anxiety disorder seems to further intensify this risk. Individuals with this constellation of diagnoses may require specialized services and multiple modalities to address both internalizing and externalizing symptoms. Adolescents with anxiety disorders and anger problems may use alcohol and drugs as a means of regulating emotions,[45] underscoring the need for early identification and treatment given the long-term adverse consequences associated with adolescent substance abuse.[46]

Developing interventions to reduce the prevalence of anger attacks and impulsive anger is of critical public health importance. Our findings suggest that such interventions would usefully be targeted at adolescents, including those with anxiety disorders. Between 60 and 80% of adolescents with an anxiety disorder report experiencing anger attacks, and about one-fifth report repeated anger attacks that are out-of control and out-of-proportion, compared with approximately 8% of adolescents without an anxiety disorder. Anxiety disorders are common[47] and frequently begin in adolescence.[47] Early adolescence is thus a critical time for the development of skills that can allow children to express and regulate their anger more adaptively. Given the high individual and societal costs associated with IED,[4] the long-term chronicity of anxiety disorders, the high prevalence of these disorders,[48] and the low likelihood of treatment or any service utilization,[1, 4] the development of prevention programs that promote adaptive expression and regulation of emotions, including anger, is an important public health priority.

Although individuals with comorbid IED and anxiety have greater impairment and increased comorbidity, they are no more likely to seek treatment, and in some cases are less likely to receive treatment. Available evidence indicates that only a minority of individuals diagnosed with IED in treatment settings were seeking treatment for their anger.[49] Moreover, symptoms of IED may be misdiagnosed or misinterpreted by both parents and clinicians as general oppositional defiance, or as symptoms of another disorder such as panic disorder. Given evidence indicates the efficacy of pharmacological treatments for aggression,[50] increasing early identification and referral to treatment of individuals with

aggressive outburst, including or not including anger, is warranted.

These results should be considered with several limitations in mind. First, all diagnoses were based on self-report using a lay-administered design. However, these instruments have well-documented reliability and validity for general population samples. We note that lifetime rates of IED are higher in NCS-A than in NCS-R; higher lifetime rates of psychiatric disorders in adolescents compared with adults have been noted extensively in the literature,[51] and are likely a combination of differential recall and sensitivity to symptoms among adolescents as well as cohort effects. Second, the NCS-R and NCS-A recruited from household and school samples, and incarcerated individuals and those with housing insecurity are not represented. Given that the prevalence of both anxiety disorders and IED is likely higher in these nonhousehold-residing populations, our estimates should be considered conservative. Further, the content and validity of the diagnosis of IED have received substantial discussion in the clinical and epidemiological literatures.[52] The diagnostic overlap with other disorders characterized by behavioral disruption (e.g., ODD, ADHD, and bipolar disorder) as well as comorbidity with disorders such as depression[53] make the validity of the IED diagnosis difficult to assess. However, other studies indicate that IED is distinguishable and unique from other disorders.[23,24] Finally, DSM-5 has narrowed the definition of IED to include recurrent attacks that occur within a year; our diagnostic algorithm included all those with recurrent attacks in their lifetime. We had limited power to assess this more narrow definition of IED, and note that there is debate over the validity of such annual versus lifetime cut-points.[4,23,54] We note that our results indicate that even with an inclusive definition of IED that allows for attacks to occur across years, we demonstrate substantial functional impairment and comorbidity, suggesting that even patients who do not meet the more narrow definition may benefit from assessment of anger and aggression.

Given the high societal and personal cost of IED and anger attacks, these results underscore the importance of identifying and treating individuals with anger issues early in the life course, especially in the context of co-occurring anxiety disorders. Taken together, we find that anger attacks and IED are common among individuals with anxiety disorders and are associated with greater anxiety-related impairment and comorbidity, yet are not related to higher levels of treatment utilization.

REFERENCES

1. McLaughlin KA, Green JG, Hwang I, et al. Intermittent explosive disorder in the National Comorbidity Survey Replication Adolescent Supplement. Arch Gen Psychiatry 2012;69:1131–1139.
2. Coccaro EF. Intermittent explosive disorder. Curr Psychiatry Rep 2000;2:67–71.
3. McCloskey MS, Kleabir K, Berman ME, et al. Unhealthy aggression: intermittent explosive disorder and adverse physical health outcomes. Health Psychol 2010;29:324–332.
4. Kessler RC, Coccaro EF, Fava M, et al. The prevalence and correlates of DSM-IV intermittent explosive disorder in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2006;63:669–678.
5. Coccaro EF, Posternak MA, Zimmerman M. Prevalence and features of intermittent explosive disorder in a clinical setting. J Clin Psychiatry 2005;66:1221–1227.
6. Kessler RC, Ormel J, Petukhova M, et al. Development of lifetime comorbidity in the World Health Organization world mental health surveys. Arch Gen Psychiatry 2011;68:90–100.
7. Kashdan TB, Collins RL. Social anxiety and the experience of positive emotion and anger in everyday life: an ecological momentary assessment approach. Anxiety Stress Coping 2010;23:259-72.
8. Moscovitch DA, McCabe RE, Antony MM, et al. Anger experience and expression across the anxiety disorders. Depress Anxiety 2008;25:107–113.
9. Kashdan TB, McKnight PE. The darker side of social anxiety: when aggressive impulsivity prevails over shy inhibition. Curr Dir Psychol Sci 2010;19:47–50.
10. Breen WE, Kashdan TB. Anger suppression after imagined rejection among individuals with social anxiety. J Anxiety Disord 2011;25:879–887.
11. Schaeffer CM, Petras H, Ialongo N, et al. Modeling growth in boys' aggressive behavior across elementary school: links to later criminal involvement, conduct disorder, and antisocial personality disorder. Dev Psychol 2003;39:1020–1035.
12. Gross JJ. Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. J Pers Soc Psychol 1998;74:224–237.
13. Galbraith T, Heimberg RG, Wang S, et al. Comorbidity of social anxiety disorder and antisocial personality disorder in the National Epidemiological Survey on Alcohol and Related Conditions (NESARC). J Anxiety Disord 2014;28:57–66.
14. Fettich KC, McCloskey MS, Look AE, Coccaro EF. Emotion regulation deficits in intermittent explosive disorder. Aggress Behav 2014. doi: 10.1002/AB.21566. [Epub ahead of print]
15. Blanchard-Fields F, Coats AH. The experience of anger and sadness in everyday problems impacts age differences in emotion regulation. Dev Psychol 2008;44:1547–1556.
16. Kashdan TB, Hofmann SG. The high-novelty-seeking, impulsive subtype of generalized social anxiety disorder. Depress Anxiety 2008;25:535–541.
17. Kessler RC, Merikangas KR. The National Comorbidity Survey Replication (NCS-R): background and aims. Int J Methods Psychiatr Res 2004;13:60–68.
18. Kessler RC, Avenevoli S, Costello EJ, et al. National comorbidity survey replication adolescent supplement (NCS-A): II. Overview and design. J Am Acad Child Adolesc Psychiatry 2009;48:380–385.
19. Kessler RC, Avenevoli S, Costello EJ, et al. Design and field procedures in the US National Comorbidity Survey Replication Adolescent Supplement (NCS-A). Int J Methods Psychiatr Res 2009;18:69–83.
20. Kessler RC, Ustun TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO)

Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res 2004;13:93–121.

21. Kessler RC, Avenevoli S, Green J, et al. National comorbidity survey replication adolescent supplement (NCS-A): III. Concordance of DSM-IV/CIDI diagnoses with clinical reassessments. J Am Acad Child Adolesc Psychiatry 2009;48:386–399.

22. Kessler RC, Abelson J, Demler O, et al. Clinical calibration of DSM-IV diagnoses in the World Mental Health (WMH) version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res 2004;13:122–139.

23. Ahmed AO, Green BA, McCloskey MS, Berman ME. Latent structure of intermittent explosive disorder in an epidemiological sample. J Psychiatr Res 2010;44:663–672.

24. McCloskey MS, Lee R, Berman ME, et al. The relationship between impulsive verbal aggression and intermittent explosive disorder. Aggress Behav 2008;34:51–60.

25. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.

26. Perlis RH, Smoller JW, Fava M, et al. The prevalence and clinical correlates of anger attacks during depressive episodes in bipolar disorder. J Affect Disord 2004;79:291–295.

27. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-Patient Edition (SCID-I/NP). New York: Biometrics Research, New York State Psychiatric Institute; 2002.

28. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry 1997;36:980–988.

29. Bird HR, Gould MS, Staghezza B. Aggregating data from multiple informants in child psychiatry epidemiological research. J Am Acad Child Adolesc Psychiatry 1992;31:78–85.

30. Braaten EB, Biederman J, DiMauro A, et al. Methodological complexities in the diagnosis of major depression in youth: an analysis of mother and youth self-reports. J Child Adolesc Psychopharmacol 2001;11:395–407.

31. Leon AC, Olfson M, Portera L, et al. Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. Int J Psychiatry Med 1997;27:93–105.

32. Kashdan TB, McKnight PE, Richey JA, Hofmann SG. When social anxiety disorder co-exists with risk-prone, approach behavior: investigating a neglected, meaningful subset of people in the National Comorbidity Survey-Replication. Behav Res Ther 2009;47:559–568.

33. Linehan MM, Bohus M, Lynch TR. Dialectical behavior therapy for pervasive emotion dysregulation. In: Gross JJ, editor. Handbook of Emotion Regulation. New York: Guilford Press; 2007:581–605.

34. Denson T. The multiple systems model of angry rumination. Pers Soc Psychol Rev 2013;17:103–123.

35. Coccaro EF, McCloskey MS, Fitzgerald DA, Phan KL. Amygdala and orbitofrontal reactivity to social threat in individuals with impulsive aggression. Biol Psychiatry 2007;62:168–178.

36. Coccaro EF. A family history study of intermittent explosive disorder. J Psychiatr Res 2010;44:1101–1105.

37. Hettema JM, Neale MC, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. Am J Psychiatry 2001;158:1568–1578.

38. Boylan JM, Ryff CD. Varieties of anger and the inverse link between education and inflammation: toward an integrative framework. Psychosom Med 2013;75:566–574.

39. Dougherty DD, Rauch SL, Deckersbach T, et al. Ventromedial prefrontal cortex and amygdala dysfunction during an anger induction positron emission tomography study in patients with major depressive disorder with anger attacks. Arch Gen Psychiatry 2004;61:795–804.

40. Monk CS, Telzer EH, Mogg K, et al. Amygdala and ventrolateral prefrontal cortex activation to masked angry faces in children and adolescents with generalized anxiety disorder. Arch Gen Psychiatry 2008;65:568–576.

41. Kimbrell TA, George MS, Parekh PI, et al. Regional brain activity during transient self-induced anxiety and anger in healthy adults. Biol Psychiatry 1999;46:454–465.

42. Marks I, Nesse RM. Fear and fitness: an evolutionary analysis of anxiety disordersq. Ethnol Sociobiol 1994;15(5-6): 247–261.

43. Cloitre M, Stovall-McClough KC, Nooner K, et al. Treatment for PTSD related to childhood abuse: a randomized controlled trial. Am J Psychiatry 2010;167:915–924.

44. Lejoyeux M, Feuche N, Loi S, et al. Study of impulse-control disorders among alcohol-dependent patients. J Clin Psychiatry 1999;60:302–305.

45. Bolton J, Cox B, Clara I, Sareen J. Use of alcohol and drugs to self-medicate anxiety disorders in a nationally representative sample. J Nerv Ment Dis 2006;194:818–825.

46. Odgers CL, Caspi A, Nagin DS, et al. Is it important to prevent early exposure to drugs and alcohol among adolescents? Psychol Sci 2008;19:1037–1044.

47. Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:593–602.

48. Kessler RC, Avenevoli S, McLaughlin KA, et al. Lifetime comorbidity of DSM-IV disorders in the US National Comorbidity Survey Replication Adolescent Supplement (NCS-A). Psychol Med 2012;42:1997–2010.

49. Zimmerman M, Mattia JI. Principal and additional DSM-IV disorders for which outpatients seek treatment. Psychiatr Serv 2000;51:1299–1304.

50. Coccaro EF, Lee RJ, Kavoussi RJ. A double-blind, randomized, placebo-controlled trial of fluoxetine in patients with intermittent explosive disorder. J Clin Psychiatry 2009;70:653–662.

51. Keyes KM, Liu C. Age, birth cohort, and period effects in psychiatric disorders in the USA. In: Koenen K, Rudenstine S, Susser E, Galea S, editors. A Life Course Approach to Mental Disorders. New York: Oxford University Press; 2014: 46–60.

52. McCloskey MS, Berman ME, Noblett KL, Coccaro EF. Intermittent explosive disorder-integrated research diagnostic criteria: convergent and discriminant validity. J Psychiatr Res 2006;40:231–242.

53. Gould RA, Ball S, Kaspi SP, et al. Prevalence and correlates of anger attacks: a two site study. J Affect Disord 1996;39: 31–38.

54. Coccaro EF, Kavoussi RJ, Berman ME, Lish JD. Intermittent explosive disorder-revised: development, reliability, and validity of research criteria. Compr Psychiatry 1998;39: 368–376.