Intermittent Explosive Disorder

Emil F. Coccaro, MD

Address
Director, Clinical Neuroscience and Psychopharmacology Research Unit, The Pritzker School of Medicine, The University of Chicago, 5841 South Maryland Avenue, Chicago, IL 60637, USA.
E-mail: ecoccaro@yoda.bsd.uchicago.edu

Current Psychiatry Reports 2000, **2**:67–71
Current Science Inc. ISSN 1523–3812

Intermittent explosive disorder (IED) may best be thought of as a categoric expression of recurrent, problematic impulsive aggressive behavior. Although diagnostic criteria issues have made systematic research in IED difficult, recent work with new research criteria may allow for important empiric work to take place. Given that previous research in the area of impulsive aggression has been highly informative concerning the genetics, biology, and pharmacologic treatment of this behavior, application and extension of this work to IED is crucial. This paper reviews several important aspects of IED including its history in the Diagnostic and Statistical Manual of Mental Disorders, the formation of new research criteria, and the phenomenologic, epidemiologic, genetic, biologic, and treatment correlates of this disorder.

Introduction

Intermittent explosive disorder (IED) is currently grouped in the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, edn 4) with a variety of other impulse control disorders. Primarily, IED is characterized by recurrent episodes of a failure to resist aggressive impulses which in turn result in serious assault against persons or in the destruction of property. Diagnostic criteria for IED have changed since the first edition of the DSM and are, for the most part, unsatisfactory for both clinical diagnostic and research purposes. This has led to controversy and little empiric research. However, the recognition that impulsive aggression, a common form of aggression, has substantial biologic and treatment correlates has led to a reassessment of IED as a diagnostic entity and as a platform from which to conduct meaningful research. This paper briefly reviews the history of IED and highlights some of the phenomenologic, biologic, and treatment correlates of this disorder, particularly as currently conceptualized in research circles.

History of Intermittent Explosive Disorder

At first, DSM highlighted “recurrent, problematic, impulsive aggressive behavior” as a diagnostic entity. Later revisions of DSM, however, progressively moved away from this position and tended to restrict "IED-type" diagnostic criteria set so that DSM criteria could not identify most individuals characterized by the type of impulsive aggression repeatedly shown to correlate with specific developmental and psychosocial variables, measures of central neurobiologic function, and responses to specific psychopharmacologic agents.

Diagnostic and Statistical Manual, editions I and II

In DSM-I, impulsively aggressive individuals were described as *passive-aggressive personality (aggressive type)*. These individuals manifested "a persistent reaction to frustration with irritability, temper tantrums and destructive behavior". In DSM-II, passive-aggressive personality (aggressive type) evolved into *explosive personality* and was described as “intermittently violent behavior occurring in an aggressive person.” These individuals were described as having "gross outbursts of rage or of verbal or physical aggressiveness which were strikingly different from the patient's usual behavior.” DSM-II also noted that these patients were "generally considered to be excitable, aggressive, and over responsive to environmental pressures.” However, in that neither DSM-I or DSM-II had specific criteria for any diagnosis, these diagnoses were not accompanied by any operational diagnostic criteria.

Diagnostic and Statistical Manual, edition III and revised edition III

In DSM-III, explosive personality was codified as IED for the first time and placed under the Axis I classification of mental disorders. In DSM-III, IED had four criteria. Regardless, these new criteria were problematic for several reasons. First, *assaultive* and *destructive* acts (criterion A) were not defined in any operational manner. Thus, it was left to clinicians to decide, without specific guidelines, what sort of behaviors were of sufficient severity to meet this criteria. Second, no minimal frequency, and no time frame, for these assaultive/destructive behaviors was set (criterion A). Thus, it was unclear how many, and in what minimal time frame, putative assaultive/destructive acts should occur before one could make a diagnosis of IED. Third, the exclusion criteria required that subjects with DSM-III IED not be generally aggressive or impulsive in between "aggressive episodes" (criterion C). This was unrealistic as many, if not most, individuals with recurrent, problematic,

Table 1. Research criteria for intermittent explosive disorder

A. Recurrent incidents of aggression manifest as verbal or physical aggression towards other people, animals, or property occurring twice weekly on average for 1 month
B. The degree of aggressiveness expressed is grossly out of proportion to the provocation or any precipitating psychosocial stressors
C. The aggressive behavior is generally not premeditated (*eg*, is impulsive) and is not committed in order to achieve some tangible objective (*eg*, money, power, intimidation, etc.).
D. The aggressive behavior causes either marked distress in the individual or impairment in occupational or interpersonal functioning
E. The aggressive behavior is not better accounted for by another mental disorder (*eg*, major depressive/manic/psychotic disorder; attention deficit hyperactivity disorder), general medical condition (*eg*, head trauma, Alzheimer's disease); or to the direct physiologic effects of a substance

(*From* Coccaro *et al.* [16].)

impulsive aggressive behaviors are generally impulsive and aggressive in between their more severe episodes of behavioral aggression. Fourth, excluding the presence of antisocial personality disorder (criterion D) similarly restricted the diagnosis. Accordingly, fulfillment of these criteria meant that DSM-III IED cannot generalize to the majority of people with problematic impulsive aggressive behavior. Revised DSM-III (DSM-III-R) criteria did not resolve these issues; DSM-III-R made it even more difficult for individuals with recurrent, problematic, impulsive aggressive behaviors to be specifically identified. This was because the exclusionary criteria (criterion D) were expanded and the presence of a borderline (in addition to an antisocial) personality disorder, also ruled out a diagnosis of DSM-III-R IED. Given that a sizable minority of subjects with problematic impulsive aggressive behaviors may also meet criteria for a borderline personality disorder, this exclusion criteria further limited the ability to generalize DSM-III-R criteria of IED. Empiric studies bare this out. In a study that strictly applied DSM-III criteria only a small percentage (*ie*, 20%) of individuals with recurrent, problematic, impulsive aggression could actually be given a diagnosis of IED based on these restrictive exclusionary criteria [1].

Diagnostic and Statistical Manual, edition IV

The DSM-IV criteria were revised again in 1994 under new editors. This revision removed the problematic "C" criterion from DSM-III/III-R and implied that individuals with DSM-IV IED could be generally impulsive or aggressive in between more severe episodes of aggressive behavior. DSM-IV also made a subtle change in the exclusionary criteria. Here the wording of the diagnostic exclusionary ("C") criteria were changed so that the aggressive behavior could "not be better explained by" another disorder. This set the stage to allow a DSM-IV diagnosis of IED to be made even in the presence of certain comorbid diagnoses to such as antisocial and borderline personality disorder (First M, DSM-IV Text Editor; Personal communication). How this distinction could be made, however, was not addressed.

Research Criteria

Despite the improvement in the IED diagnostic criteria set for the DSM-IV, significant problems remain. These relate to the lack of specificity as to the nature, frequency, and consequences of the recurrent aggressive behavior. In addition, current DSM-IV criteria do not operationalize 1) the frequency of aggressive behaviors, 2) the time period in which these behaviors occur, and 3) the severity of the behaviors; and do not require 1) that the behavior be impulsive in nature or, 2) the presence of distress or functional impairment.

Currently published research criteria for IED (Table 1) are expected to evolve into the DSM-V criteria set for IED, planned for publication sometime in 2000. These research criteria for IED involve five aspects that critically operationalize the criteria for IED. First, they broaden the scope of aggressive behavior encompassed by the IED diagnosis by including verbal and indirect physical aggression (provided that these behaviors are impulsive, frequent, and associated with distress or impairment). Less severe impulsive aggressive behavior is now included because these forms of aggression have been shown to be significantly reduced in impulsive aggressive subjects in double-blind, placebo-controlled clinical trials with fluoxetine [2,3]. Second, they require the specified aggressive behavior to be impulsive in nature. If the presence of impulsive aggression is not stipulated, individuals with premeditated (*ie*, criminal) aggression could be diagnosed with IED. Inclusion of premeditated aggression in IED would make the diagnosis nonspecific because existing data strongly suggests a psychosocial [4], biologic [5,6] and treatment response [7,8] distinction between impulsive and premeditated aggression. Third, they require a minimal frequency over time, which is critical in order to make the diagnosis of IED reliable across clinicians and to ensure that subjects with only occasional impulsive aggressive outbursts (especially those of low severity) are not assigned this disorder. Fourth, they require the presence of subjective distress (*eg*, in the individual), social or occupational dysfunction. This formally focuses the concept of IED as a behavioral disorder and further enables the criteria to rule out subjects for whom

their impulsive aggressive behavior is not functionally severe enough, and again, not to overdiagnose this disorder. Fifth, they modify the diagnostic exclusionary criteria to 1) allow subjects with antisocial or borderline personality disorder (ASPD/BPD) to be given IED and, 2) rule out subjects with current histories of major depression. The former modification is made for two reasons. One, impulsive aggressive subjects with ASPD or BPD would not be identified by IED criteria. It is understood that the presence of ASPD or BPD appears to be a justifiable exclusion criteria for IED. Because BPD subjects are impulsive and prone to angry outbursts, and ASPD subjects are often irritable and aggressive, why use two diagnoses to describe the same person? However, many ASPD/BPD subjects are not particularly impulsive aggressive. Two, there are few data to support the idea that impulsive aggressive behavior should be hierarchically placed under the constructs of ASPD/BPD. Familial [9], twin [10], biologic [11,12], and treatment response [3,7,8,13,14], data suggest that impulsive aggressive behavior, although present in many ASPD/BPD subjects, has specific clinical relevance apart from the remaining diagnostic features of these personality disorders. The latter modification regarding the exclusion of major depressive disorder was made to formally recognize the fact that impulsive aggressive outbursts are characteristic of a number of individuals suffering from a current major depressive disorder [15]. Although it is possible that these outbursts identify a clinically meaningful subgroup of depressives, it is widely appreciated that the presence of major depression is associated with irritability, a behavioral symptom manifested by quickness to react to aversive stimuli with negative affect. In fact, the presence of irritability was part of the "A" criterion in the research diagnostic criteria (RDC, the precursor to the DSM-III) set for major depressive disorder. Moreover, a reduction in irritability scores is usually noted with successful psychopharmacologic treatment of major depression.

Research diagnoses of IED can be made with good reliability ($\kappa = 0.87$) and subjects with IED demonstrate higher scores on measures of aggression and impulsivity when compared with comparable subjects without a research diagnosis of IED. Subjects with IED also have lower global functioning than subjects without IED. Notably, this difference in global function disappears when aggression and impulsivity scores are factored into the statistical model suggesting that the reduced psychosocial functioning of the IED subjects could be attributed to the presence of impulsive aggression [16].

Phenomenology

There is general consistency in the descriptions of subjects with IED regardless of which specific diagnostic criteria set is used. First, IED appears to begin as early as childhood [17] or adolescence with a mean age of onset at 15 years and an average duration of about 20 years [18]. Second, IED occurs more commonly in males, with a male:female ratio of 3:1. Third, aggressive outbursts are described as having a rapid onset [18], often without a noticeable prodromal period [1,17], short-lived (< 30 min) [18], involving verbal, destructive and nondestructive property assault, and physical assault [17,18], and associated with substantial distress [18] and impairment in social functioning [17,18], occupational functioning, and legal/financial problems [18]. Aggressive outbursts most commonly occur in response to a minor provocation by a close intimate or associate [1,18], although, in some cases they may appear to occur without identifiable provocation [18]. In between more severe assaultive and destructive episodes, many IED subjects, as suggested by our own data, also have less severe aggressive episodes manifested by verbal or nondestructive property assault [16,18].

Epidemiology

Despite epidemiologic data suggesting that recurrent, problematic, impulsive aggressive behavior is far from rare, there have been no population-based epidemiologic surveys of IED to date. However, Zimmerman *et al*. [19] reported on a large clinical survey using current DSM-IV (not research) IED criteria in a sample of 748 psychiatric outpatients. In this survey, using trained raters and semi-structured interviews for both Axis I and II conditions, lifetime diagnosis of IED by current DSM-IV criteria was reported at 6.8%. Closer examination of the raw unpublished data reveals that allowing for the presence of antisocial and borderline personality disorder (*ie*, using IED research criteria) increases the lifetime rate of IED to 13.2% in this sample. Of course, estimating the prevalence of IED (or of recurrent, problematic, impulsive aggressive behavior) in the community from these clinical data is difficult. However, considering that the median rate of BPD in the community has been reported at 1.6% [20] and that the rate of BPD in the Zimmerman *et al*. [19] sample was 12% (*note*, a community sample to clinical sample ratio of 0.133), it is possible that the community rate of DSM-IV IED could be approximately 0.9% (*ie*, 6.8% $\times$ 0.133) and that the rate of IED by research criteria (at least by simply allowing comorbid diagnoses of AsPD and BPD) could be approximately 1.8% (*ie*, 13.2% $\times$ 0.133). If so, nearly 2.5 million individuals in the United States could have a lifetime diagnosis of IED by current DSM-IV criteria; and nearly 5 million by research criteria.

Biologic and Treatment Response Correlates

Nearly all studies in this area focus on aggression as a dimensional, as opposed to a categoric, variable. However, since the development of research criteria for IED we have had the opportunity to explore biologic and treatment response correlates in our ongoing studies. For

example, we have found in our pilot data that the maximal prolactin response to d-fenfluramine challenge is reduced in subjects meeting our research criteria for IED. Preceding our fenfluramine challenge studies, Linnoila *et al*. [5] and Virkunnen *et al*. [6], reported reduced CSF 5-HIAA concentrations in subjects diagnosed as DSM-III IED compared with subjects who were not IED or those who demonstrated nonimpulsive aggression. Regarding treatment response, it is noteworthy that all subjects in our recently published fluoxetine trial of impulsive aggression met research criteria for IED [3]. Accordingly, these data demonstrate that the core features of IED are responsive to pharmacologic treatment, most notably (*ie*, serotonergic) to a treatment which works through a neurobiologic system already shown to influence impulsive aggressive behavior. Pharmacologic response data are also consistent with the hypothesis that impulsive IED subjects respond to pharmacologic intervention. In their study, Barratt *et al*. [8] demonstrated that impulsive, but not nonimpulsive, aggressive behavior is reduced by the anticonvulsant, phenylhydantoin. Although this group did not use research criteria for IED (the study was completed before these criteria were proposed), all impulsive aggressive subjects in their sample would have met research criteria for IED.

Behavioral Genetics

Although there are no twin or adoption studies of IED, existing family history data suggests that IED or IED-type behavior is familial. Two studies in the 1970s report that first-degree relatives of patients with histories of violent behavior have a high incidence of violent behavior [21,22]. Another study conducted a decade later, reported that the frequency of first-degree relatives with a history of "temper outbursts" (defined as the first two DSM-III criteria for IED) was reported as increased in psychiatric patients with a personal history of these behaviors compared to patients without this history (18.2% vs 4.3%, $P < 0.01$, OR = 4.23) [23]. Similarly, there was a strong trend for the familial aggregation of IED (6.8% vs 0%, $P < 0.06$) in patients with temper outbursts. Most recently, we conducted a blinded, controlled, family history study using research criteria for IED and found a significantly elevated morbid risk of IED in first-degree relatives of IED Probands compared with control probands (26% vs 8.0%; OR = 3.25). Notably, this elevation in the morbid risk of IED was not due to comorbidity of BPD/ASPD or to a life history of major depression, alcohol/drug use disorder, or suicidal behavior in the IED probands or in the relatives of the IED probands. These findings, which need to be replicated in a family study (*ie*, where each family member is interviewed about themselves), strongly suggest that IED, as defined by research criteria, is familial and phenomenologically independent of other conditions.

Molecular Genetics

The molecular genetics of impulsive aggression and IED is currently emerging with rise of association studies involving various DNA polymorphisms of candidate genes. Association studies are conducted in order to gain insight as to where approximately in the genome one may find genes of relevance to a phenotype (*eg*, impulsive aggression). Because polymorphisms of candidate genes (*ie*, genes whose products should be involved in physiologically relevant functions of central neurotransmitters) are used, the search for the approximate loci of relevant genes is narrowed. If the polymorphism is a coding region variant, positive association with a behavior or phenotype suggests a direct link to a genetic abnormality. If the poylmorphism is not a coding region variant (*eg*, is intronic), positive association suggests an indirect link (linkage disequilibrium) to a genetic abnormality. This finding may then be followed up for further investigation and ultimate identification of a gene relevant for the phenotype or behavior in question.

One of the first notable studies in this area was that of Brunner *et al*. [24], which reported an association between a point mutation for the *MAO-A* gene in an extended family pedigree and impulsive violence in males with low intelligence. The presence of this mutation was associated with evidence altered catecholamine metabolism (*ie*, reduced brain catecholamine breakdown and increased activity at central catecholamine receptors). Although no other families with this specific *MAO-A* point mutation have been reported, this report highlighted the potential of the candidate gene approach to the molecular genetics of aggression. At about the same time, Nielson *et al*. [25] reported that the presence of the L allele for the (intronic) biallelic TPH polymorphism was associated with a reduction of CSF 5-HIAA concentration in impulsive violent offenders (nearly all with DSM-III IED). In the same study, the presence of the L allele was also associated with history of suicide attempts in all violent offenders. Although this was not replicated by Abbar *et al*. [26], using a different TPH polymorphism, Nielson *et al*. [27], did replicate this finding in a second group of violent offenders, specifically in impulsive violent offenders and more specifically for severe suicide attempts. Linkage for this TPH polymorphism was also noted in a sib-pair analysis in this same report. At the same time, Lappalainen *et al*. [28] reported an association between antisocial alcoholism (*ie*, alcoholism with antisocial personality disorder or DSM-III IED) and the C allele biallelic polymorphism for the 5-HT-1d-Beta receptor.

Conclusions

Although IED has been poorly characterized over the years, the behavioral phenomena underlying this disorder (*ie*, impulsive aggression) have been well studied for a number of years. This research has led to important insights into the biology and treatment of impulsive aggressive behavior [29]. With several psychopharmacologic options available

to treat recurrent, problematic, impulsive aggression now available (*eg*, SSRIs, mood stabilizers, etc.), IED should now be systematically investigated so that patients with this disorder can be offered potentially efficacious treatments (psychopharmacologic or cognitive-behavioral treatments) and can be identified for further research in this area.

References

1. Felthous AR, Bryant G, Wingerter CB, Barratt ES: **The diagnosis of intermittent explosive disorder in violent men.** *Bull Am Acad Psychiatry Law* 1991, **19:**71–79.
2. Salzman C, Wolfson AN, Schatzberg A, *et al.*: **Effect of fluoxetine on anger in symptomatic volunteers with borderline personality disorder.** *J Clin Psychopharmacol* 1995, **15:**23–29.
3. Coccaro EF, Kavoussi RJ: **Fluoxetine and impulsive aggressive behavior in personality disordered subjects.** *Arch Gen Psychiatry* 1997, **54:**1081–1088.
4. Dodge KA, Pettit G, Bates J: **Socialization mediators of the relation between socioeconomic status and child conduct problems.** *Child Dev* 1994, **65:**649–665.
5. Linnoila M, Virkkunen M, Scheinin M, *et al.*: **Low cerebrospinal fluid 5-hydroxylndolacetic acid concentration differentiates impulsive from nonimpulsive violent behavior.** *Life Sci* 1983, **33:**2609–2614.
6. Virkkunen M, Rawlings R, Tokola R, *et al.*: **CSF biochemistries, glucose metabolism, and diurnal activity rhythms in alcoholic, violent offenders, fire setters, and healthy volunteers.** *Arch Gen Psychiatry* 1994, **51:**20–27.
7. Sheard M, Manini J, Bridges C, Wapner A: **The effect of lithium on impulsive aggressive behavior in man.** *Am J Psychiatry* 1976, **133:**1409–1413.
8. Barratt ES, Stanford MS, Felthous AR, Kent TA: **The effects of phenytoin on impulsive and premeditated aggression: A controlled study.** *J Clin Psychopharmacology* 1997, **17:**341–349.
9. Silverman JM, Pinkham L, Horvath TB, *et al.*: **Affective and impulsive personality disorder traits in the relatives of borderline personality disorder.** *Am J Psychiatry* 1991, **148:**1378–1385.
10. Torgerson S: **Genetic and nosological aspects of schizotypal and borderline personality disorder.** *Arch Gen Psychiatry* 1984, **41:**546–554.
11. Coccaro EF, Siever LJ, Klar HM, *et al.*: **Serotonergic studies in affective and personality disorder: Correlates with suicidal and impulsive aggressive behavior.** *Arch Gen Psychiatry* 1989, **46:**587–599.
12. Moss HB, Yao JK, Panzak GL: **Serotonergic responsivity and behavioral dimensions in antisocial personality disorder with substance abuse.** *Biol Psychiatry* 1990, **28:**325–338.
13. Cowdry RW, Gardner DL: **Pharmacotherapy of borderline personality disorder: Alprazolam, carbamazepine, trifluroperazine, and trancypromine.** *Arch Gen Psychiatry* 1988, **45:**111–119.
14. Linehan MM, Tutek DA, Heard HL, Armstrong HE: **Interpersonal outcome of cognitive behavioral treatment for chronically suicidal borderline patients.** *Am J Psychiatry* 1994, **151:**1771–1776.
15. Fava M, Rosenbaum JF, Pava JA, *et al.*: **Anger attacks in unipolar depression, part 1: Clinical correlates and response to fluoxetine treatment.** *Am J Psychiatry* 1993, **150:**1158–1163.
16. 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.
17. Mattes JA: **Comparative effectiveness of carbamazepine and propranolol for rage outbursts.** *J Neuropsychiatry Clin Neurosci* 1990, **2:**159–164.
18. McElroy SL, Soutullo CA, Beckman DA, *et al.*: **DSM-IV intermittent explosive disorder: A report of 27 cases.** *J Clin Psychiatry* 1998, **59:**203–210.
19. Zimmerman M, Mattia J, Younken S, Torres M: *The prevalence of DSM-IV Impulse Control Disorders in Psychiatric Outpatients. APA New Research Abstracts #265*. Washington, DC: APA Press; 1998.
20. Lyons MJ: **Epidemiology of Personality Disorders.** In In *Textbook in Psychiatric Epidemiology.* Edited by Tsuang MT, Tohen M, Zahner GEP. New York: Wiley-Liss; 1995:407–436.
21. Bach-Y-Rita G, Lion JR, Climent CF, Ervin F: **Episodic dyscontrol: A study of 130 violent patients.** *Am J Psychiatry* 1971, **127:**1473–1478.
22. Maletsky BM: **The episodic dyscontrol syndrome.** *Dis Nervous System* 1973, **36:**178–185.
23. Mattes JA, Fink M: **A family study of patients with temper outbursts.** *J Psychiatr Res* 1987, **21:**249–255.
24. Brunner HG, Nelen M, Breakefeld XO, *et al.*: **Abnormal behavior associated with a point mutation in the structural gene for monoamine oxidase A.** *Science* 1995, **262:**578–580.
25. Nielson DA, Goldman D, Virkkunen M, *et al.*: **Suicidality and 5-hydroxyindolacetic acid concentration associated with a tryptophan hydoxylase polymorphism.** *Arch Gen Psychiatry* 1994, **51:**34–38.
26. Abbar M, Courtet P, Amadeo S, *et al.*: **Suicidal behaviors and the tryptophan hydroxylase gene.** *Arch Gen Psychiatry* 1995, **52:**846–849.
27. Nielson DA, Virkkunen M, Lappalainen J, *et al.*: **A tryptophan hydroxylase gene marker for suicidality and alcoholism.** *Arch Gen Psychiatry* 1998, **55:**593–602.
28. Lappalainen J, Long JC, Eggert M, *et al.*: **Linkage of antisocial alcoholism to the serotonin 5-HT-1B receptor gene in two populations.** *Arch Gen Psychiatry* 1998, **55:**989–994.
29. Coccaro EF: **Central neurotransmitter function in human aggression.** In In *Neurobiology and Clinical Views on Aggression and Impulsivity.* Edited by Maes M, Coccaro E. New York: J Wiley & Sons; 1998:143–168.