Intermittent Explosive Disorder

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Glossary

Diagnostic and Statistical Manual (DSM) – Published by the American Psychiatric Association. In the United States, it is the primary system used to classify and diagnose mental disorders. It is currently in its fourth edition (DSM-IV).

Epiphenomenon – A secondary phenomenon that occurs alongside or in parallel to a primary phenomenon, but may not be causally linked to the primary phenomenon.

First line – Preferred, standard, or initially recommended approach; often used in reference to treatment selection.

Impulsive aggression – Also known as reactive or hostile aggression, impulsive aggression occurs in response to angering thoughts. The goal of impulsive aggression is to cause harm to another. This is in contrast to instrumental or premeditated aggression in which anger is not the primary motivator for the aggressive behavior and the aggression is seen merely as a means to an end (e.g., hitting someone to steal their wallet).

Morbid risk – The probability that an individual born into a population or group will develop a disorder.

Selective serotonin reuptake inhibitors (SSRIs) – A class of drugs that increase the amount of serotonin available in the synapse (space between nerve cells) by inhibiting the recapture or reuptake of serotonin by the nerve cells that released the serotonin into the synapse.

Intermittent explosive disorder (IED) is a DSM-IV diagnosis that describes the pathology of people with aggression, typically impulsive aggression. Although aggressive behavior is relatively common, many clinicians and researchers rarely consider the diagnosis of IED when faced with a patient with recurrent, problematic, aggressive behavior. This is notable because IED has been a part of the DSM since its third edition in 1980. Before that, this construct was referred to as 'passive-aggressive personality (aggressive type)' and was characterized as "persistent reaction to frustration with irritability, temper tantrums and destructive behavior." This disorder evolved into 'explosive personality' in DSM-II at which time such patients were characterized as being aggressive individuals who display intermittently violent behavior and who are "generally excitable, aggressive, and overresponsive to environmental pressures" with "gross outbursts of rage or of verbal or physical aggressiveness different from their usual behavior." In DSM-III, 'explosive personality' was codified and operationalized as IED for the first time and assigned 'clinical disorder' status under Axis I. The diagnostic criteria, however, were not well operationalized (e.g., criterion A 'assaultive' and 'destructive' acts had no specific guidelines on which behaviors would satisfy the criteria from a severity, frequency, or time-frame standpoint) and were otherwise problematic. Subjects who were generally aggressive or impulsive in between the ill-defined aggressive episodes were excluded from receiving the diagnosis (criterion C). Since individuals with recurrent, problematic, impulsive aggression are also generally impulsive and aggressive between more severe outbursts, this exclusion ruled out the vast majority (e.g., 80%) of individuals who now would be diagnosed with IED.

With the introduction of the DSM-IV in 1994, the earlier exclusionary C criterion that omitted individuals with chronic aggression problems (effectively excluding most subjects now considered to meet criteria for IED) was removed. Regardless, DSM-IV still lacked objective criteria for the intensity, frequency, and nature of aggressive acts to meet criteria for IED (**Table 1**).

Noting the limitations of the DSM-IV criteria for IED, some investigators developed an alternative criteria set that integrated their research findings with DSM conceptualizations of IED (**Table 2**) 'integrated research' criteria for IED (IED-IR) differ from DSM-IV IED criteria on four key points. (1) IED-IR criteria operationalizes the severity and frequency of aggressive behavior required for the diagnosis. The inclusion of verbal aggression within the IED-IR construct reflects data showing that frequent verbal aggression occurs in over 85% of subjects with physical aggression, that subjects with frequent verbal aggression in the absence of more severe assaultive acts show the same core deficits and impairment as assaultive subjects and that anti-aggressive responses to serotonin reuptake inhibitors are seen in both groups. (2) IED-IR criteria explicitly require the aggressive behavior to be impulsive in nature. This was also informed by research showing psychosocial, biological, and treatment-response characteristics differentiated impulsive and premeditated aggression. (3) IED-IR

Table 1 DSM-1V criteria for intermittent explosive disorder

A. Several discrete episodes of failure to resist aggressive impulses that result in serious assaultive acts or destruction of property.
B. The degree of aggressiveness expressed during the episodes is grossly out of proportion to any precipitating psychosocial stressors.
C. The aggressive episodes are not better accounted for by another mental disorder (e.g., antisocial personality disorder, borderline personality disorder, a psychotic disorder, a manic episode, conduct disorder, or attention-deficit/hyperactivity disorder) and are not due to the direct physiological effects of a substance (e.g., a drug of abuse and a medication) or a general medical condition (e.g., head trauma and dementia of the Alzheimer's type).

Table 2 Research criteria for IED: IED-IR

A.	Recurrent incidents of aggression manifest as either: A1. Verbal or physical aggression towards other people, animals,or property occurring twice weekly on average for one month. or A2. Three episodes involving physical assault against other people or destruction of property over a one year period.
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 (e.g., is impulsive) and is not committed in order to achieve some tangible objective (e.g., 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 (e.g., major depressive/manic/psychotic disorder; ADHD); general medical condition (e.g., head trauma, Alzheimer's Dx); or to the direct physiological effects of a substance.

criteria explicitly require the presence of subjective distress (e.g., in the individual) and/or social or occupational dysfunction in order to specifically link distress/dysfunction to aggressive behavior. (4) IED-IR criteria allow subjects with borderline and/or antisocial personality disorder (BPD/AsPD) to have a comorbid IED diagnosis (i.e., if they otherwise meet the IED-IR criteria, see below). This decision was based on the finding that IED subjects with or without BPD/AsPD are similarly aggressive, and much more aggressive, than non-IED subjects with or without BPD/AsPD. Accordingly, high levels of aggression have been found to be associated with the presence of IED but not the presence of BPD/AsPD. These research criteria for IED have been used in studies of IED in several sites in the United States. Moreover, several of the suggested changes made by 'Research criteria' have been adopted in the text revisions of the current DSM-IV text revision.

Clinical Picture and Course of Illness

Prevalence

Initially IED was described as rare. However, this designation was based on limited empirical research. Four recently published epidemiological studies report that approximately 4–6% of individuals meet lifetime criteria for IED, and 1-month and 1-year point prevalence estimates of IED have been reported to be in the 2–3% range. If so, approximately 16 million Americans have met lifetime criteria for IED, and as many as 6 million or 10 million have met criteria in any 1 month or year, respectively.

Clinical Presentation

Aggressive outbursts in IED have a rapid onset, often without a recognizable prodromal period. Episodes are short-lived – typically less than 30 min – and involve verbal assault, destructive and nondestructive property assault, or physical assault. Aggressive outbursts most commonly occur in response to a minor provocation by a close intimate or associate, and IED subjects may have less severe episodes of verbal and nondestructive property assault in between more severe assaultive/destructive episodes. Episodes are associated with substantial distress, impairment in social functioning, occupational difficulty, and legal or financial problems. In a recent community sample study of more than 9200 individuals, subjects meeting current IED criteria (i.e., defined as three high-severity episodes in the current year) were found to engage in direct interpersonal aggression (67.8%), threatened interpersonal aggression (20.9%), and aggression against objects (11.4%). These subjects reported engaging in, on average, 28 high-severity aggressive acts during their worst year, with two to three lifetime aggressive outbursts requiring medical attention. Mean dollar value of property damage due to IED aggressive outbursts lifetime was approximately $1600.

Clinical Example

Roger is a 28-year-old married man who works as a community outreach provider. He was self-referred for anger problems after he found his 4-year-old daughter crying in her room in the wake of a heated argument between Roger and his wife in which Roger punched a wall. Roger acknowledged always being hot tempered, providing examples of getting into shoving matches and two fistfights when playing sports, as well as frequent aggressive behavior (honking horn, screaming at drivers, flipping them off) when driving. His aggressive behavior worsens when he is intoxicated, and he has a history of alcohol abuse. He significantly reduced his alcohol use after the birth of his daughter; despite this he continues to have problems with aggressive behavior. Roger has had to replace his cell phone twice in the past year due to him throwing it in anger. Roger also continues to verbally snap and yell at his wife and occasionally his daughter, which has placed stress on an otherwise happy marriage. He understands that his behavior is excessive, and afterwards often feels guilty and remorseful, but he adds that his anger feels overwhelming at times and that the does not know how to control it.

Quality of Life

High levels of hostility and aggression negatively impact quality of life across several dimensions, including interpersonal relationships, sleep quality, job satisfaction, and health problems. Similarly, the limited data suggest that individuals with IED have more health problems, are more impaired in overall functioning, and are less happy than healthy volunteers or psychiatric controls. Furthermore, their quality of life improves after successful treatment. There are little data on the impact of IED on the quality of life for family members. However, multiple studies have linked witnessing and experiencing aggression in childhood with adverse adult consequences, including intergenerational transmission of aggression.

Age of Onset, Gender and SES

IED appears as early as childhood and peaks in mid-adolescence with a mean age of onset in three separate studies ranging from 13.5 to 18.3 years. In one study, the age of onset was found to occur at a significantly earlier time in males as compared to females. While IED may be more common in males, recent data suggest that IED may occur with a more equal prevalence among men and women. In a large epidemiological survey, sociodemographic variables (e.g., sex, age, race, education, marital, occupational status, and family income) did not differ as a function of IED status.

Comorbidity

Available data suggest that IED is a chronic disorder whose onset precedes other comorbid Axis I disorders. If so, it is unlikely that IED develops into another disorder. More likely, IED promotes the development of other disorders by leading to divorce, financial difficulties, and stressful life experiences that promote onset of other disorders later on in adulthood. In clinical samples, IED has been reported to be highly comorbid with multiple Axis I disorders, including mood disorders, anxiety disorders, and alcohol and other substance-use disorders. In community samples, however, the relationship between current IED and such disorders was only significant for generalized anxiety disorder, alcohol abuse, and any substance-use disorder. The vast majority of subjects reported that IED began at an earlier age than these comorbid conditions.

Familial Correlates

A family history study comparing first-degree relatives of 30 IED, and 20 control, probands found significantly elevated morbid risk for IED in relatives of IED, compared to control, probands (0.26 vs. 0.08, $p < 0.01$). Elevation in the morbid risk for IED was not caused by the presence or absence of comorbid conditions among the IED probands (e.g., history of suicide attempt, major depression, alcoholism, and drug use disorder) and was not due to increases in morbid risk of other non-IED disorders in the relatives (e.g., major depression, alcoholism, drug use disorders, anxiety disorder, any disorder). Accordingly, familial aggregation of IED is not due to an epiphenomenon of the liability of either the proband or the relative to having non-IED comorbid conditions and suggests a clear familial signal. This supports research showing that aggressive behavior is under a substantial degree of genetic influence.

Biology

While laboratory studies clearly show a biobehavioral relationship between aggression and selected brain chemicals (e.g., serotonin), studies in IED, specifically, have been conducted only over the past few years. To date, published data have reported IED subjects as having altered serotonin function compared with non-IED subjects or healthy control subjects. Other studies supporting the IED–serotonin link demonstrate a reduction in: (1) prolactin responses to d-fenfluramine challenge in IED subjects compared with non-IED or healthy control subjects and (2) numbers of platelet 5-HT transporters (via H^3-paroxetine binding) in IED subjects compared with non-IED or healthy control subjects. These findings are supported by imaging studies. Two fluoro-deoxy-glucose

(FDG) positron emission tomography (PET) studies found low FDG utilization after d,l-fenfluramine challenge in frontal areas of the brain and low FDG utilization after *meta*-chlorophenylpiperazine (*m*-CPP) challenge in the anterior cingulate in IED subjects compared with healthy control participants. A third, ligand-binding study of the serotonin (5-HT) transporter also reports reduced low 5-HT transporter availability in the anterior cingulate in IED versus control subjects. Finally, a functional magnetic resonance imaging (fMRI) study demonstrated increased activation of amygdala, and reduced activation of orbital medial prefrontal cortex, to anger faces in IED subjects as compared to healthy control subjects.

Treatment of IED

Psychopharmacological treatment

Classes of agents shown to have anti-aggressive effects in double-blind, placebo-controlled trials of individuals with primary aggression (i.e., not secondary to psychosis, severe mood disorder, or organic brain syndromes) include mood stabilizers (e.g., lithium), 5-HT reuptake inhibitors (e.g., fluoxetine), and anticonvulsants (e.g., diphenylhydantoin and carbamazepine). While noradrenergic (NE) beta-blockers (e.g., propanolol/nadolol) have also been shown to reduce aggression, these agents have exclusively been tested in patient populations with secondary aggression (e.g., mental retardation, organic brain syndromes, etc.). Classes of agents which may have pro-aggressive effects include tricylic antidepressants (e.g., amitriptyline), benzodiazepines, and stimulant and hallucinatory drugs of abuse (e.g., amphetamines, cocaine, and phencyclidine). Double-blind, placebo-controlled, clinical trials suggest that anti-aggressive efficacy is specific to impulsive, rather than nonimpulsive, aggression.

A double-blind, placebo-controlled trial of fluoxetine on impulsive aggressive behavior in 100 subjects with IED (by research criteria) demonstrated anti-aggressive efficacy for fluoxetine over placebo. This study observed reduction in overt aggressive behavior as reported by subjects, subjective/objective anger/aggression, and a response rate of 70% (CGI scores of much improved or very much improved). Notably, fluoxetine was not associated with any increase in aggression compared with those randomized to placebo. In contrast, placebo was associated with a greater frequency of increased aggression, and increased magnitude of aggression, after randomization compared with fluoxetine treated subjects. While positive in result, only 29% of IED subjects displayed no aggression at end of trial. This indicates that while fluoxetine can reduce impulsive aggressive behavior, remission from IED symptoms may take more than the drug itself. Another placebo-controlled study of IED involving divalproex reported a favorable effect of this agent on overt aggression but only in IED subjects with comorbid cluster B personality disorder.

Psychotherapeutic Treatments

The authors recently completed a psychotherapy outcome study comparing the efficacy of a 12-week multicomponent CBT treatment presented in either group or individual format to a wait-list control group in the treatment of IED ($N = 45$). The treatment was modeled after the Cognitive Restructuring, Relaxation and Coping Skills Training (CRCST) treatment developed to treat anger, but was modified to serve as a more appropriate treatment for aggressive individuals (e.g., extend treatment from 8 to 12 session, include a time-out technique, and increase the emphasis on the prevention of and relapse to aggression). Aggression, anger, and associated symptoms were assessed at baseline, mid-treatment, posttreatment, and 3-month follow-up. Relative to the wait-list condition, both group and individual CRCST improved anger control and reduced aggression, anger, hostile thinking, and depressive symptoms. Posttreatment effect sizes were large and were maintained at 3-month follow-up, providing initial support for the efficacy of CBT in the treatment of IED.

Other Issues Regarding Treatment of IED

There have been no published studies regarding length of treatment for IED. Our experience is that impulsive aggression is a trait that can be suppressed, but not eliminated, by medication. We have found that within about 1 month of discontinuing fluoxetine that patients with impulsive aggressive behavior often demonstrate a return of impulsive aggressive behavior to pretreatment levels. The one study that examined the effect of lithium on impulsive aggression in prison inmates found that impulsive aggressive behavior returned to pretreatment level within 1 month of being switched to placebo. This finding contrasts with our findings with CRCST. CRCST effects continue at least 3 months after active treatment has ended, probably because treatment components (relaxation training, cognitive restructuring, and coping skills training) have been incorporated into the individual's life and are still active. In contrast, once medication is no longer in the body, its effects on behavior typically end.

There have been no published studies regarding the effect of combining modalities of treatment. Examining our own data with fluoxetine and CRCST in IED subjects, we note that both modalities yield a similar magnitude of improvement in outcome measures (e.g., ~30% remission and ~15% partial remission from IED). Since these two modalities work through different mechanisms, we would hypothesize that together they would be more effective than either alone. Our clinical

experience is consistent with this idea but these data are anecdotal. Whether medication or CRCST should be first-line may depend, in part, on the patient since some prefer medication (some individuals perceive this as easier) and others prefer psychotherapeutic treatment (some individuals wish to avoid being placed on medication). Severity of aggression may also influence choice of modality and one can envision medication (and/or both medication and CRCST) as being first-line in cases of severe aggressive behavior. While an attractive strategy, there are no currently little empiric data to support either approach at this time.

See also: Neural and Pharmacological Substrates of Aggression; Neural Bases of Defensive Aggression; Offensive and Defensive Aggression; Social Competition and Conflict Resolution.

Further Reading

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