Intermittent Explosive Disorder

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Intermittent Explosive Disorder

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INTRODUCTION

Intermittent explosive disorder (IED) was once considered a rare disorder; however, recent studies have indicated that IED is much more prevalent than previously thought. IED is associated with a high degree of social impairment. In a study of 253 individuals in a community sample diagnosed with IED, 81.3% reported psychosocial difficulties, 50% admitted to difficulties within their life due to their behavior, and 62.5% noted significant difficulties with relationships. IED may lessen in intensity as individuals become older.

Diagnosis is difficult, in part due to the vagueness of the DSM diagnostic criteria. Further, the paucity of IED studies makes identifying and treating IED a challenge. Despite these limitations, physicians must assess these impulsive and aggressive patients and be aware of available treatment options for these individuals.

DIAGNOSTIC AND ASSOCIATED FEATURES

IED is characterized by short-lived episodes of impulsive aggression that are substantially out of proportion to the inciting stressor, resulting in destruction of property or serious assaultive acts. IED is currently listed in the DSM-IV under impulse-control disorders not elsewhere classified. Diagnostic criteria and the name of the disorder have changed over time. In DSM-I, IED was referred to as passive-aggressive personality, aggressive type, and in DSM-II, IED was termed explosive personality disorder. It was not until DSM-III that the term IED was used; however, the DSM-III criteria excluded patients with antisocial personality disorder and generalized aggression or impulsivity, and in the DSM-III-R, patients with borderline personality disorder were excluded.

The DSM-IV criteria for diagnosing IED no longer excludes patients with impulsivity or generalized aggression but includes the criterion that another mental disorder, substance abuse, or general medical condition must not better account for the aggressive acts (Table 1). Impulsive aggression is not unique to IED and can be seen in multiple psychiatric and medical conditions. Thus, IED is a diagnosis of exclusion. Of note, some studies use terms such as “episodic dyscontrol” or “rage attacks” to describe aggression, making it difficult to pinpoint how many patients meet the criteria for IED. In addition, some doubt that IED is an actual diagnosis and believe that impulsive aggression is a symptom that can be experienced in multiple diseases.

The aggressive episodes are often described by patients as “spells” or “attacks,” and the symptoms often appear and resolve in minutes to hours. Symptoms have been described as an “adrenaline rush” or “seeing red.” As with other impulse-control disorders, there is often a feeling of release of tension after the episode. Aggression related to IED is often ego-dystonic and patients feel a sense of remorse and regret after the aggressive act. In a study of 27 patients who met current or past DSM-IV criteria for IED, 33% complained of physical autonomic symptoms such as palpitations, tingling, and tremor prior to the episode, and 52% complained of a change in their level of awareness.

In a study of 443 violent men, those who met DSM-III criteria for IED (n = 15) felt that an intimate partner would most likely provoke them. Their attacks usually occurred without warning, and all of the men denied wanting the outburst to occur prior to the episode. Men often attempted to console their victim after their rageful outburst.

Impulsive aggression often has different motivations. If motivation includes monetary gain, vengeance, self-defense, social dominance, expressing a political statement, or when it occurs as a part of gang behavior, IED should not be the diagnosis. The impulsive aggression seen in IED is not the same as the willingly performed and thought out aggression often seen in criminal behavior. Thus, when behavior is premeditated, individuals should not be diagnosed with IED.

Because DSM-IV exclusion criteria created difficulties in diagnosing IED, integrated research criteria (IED-IR) have been formed. A study that examined the convergent and discriminate validity of the IED-IR criteria found that IED-IR individuals who met DSM-IV diagnostic criteria for IED were no more aggressive or impaired than IED-IR individuals who did not meet these criteria.

In another attempt to clarify diagnostic
criteria for IED, an interview module for IED (IED-M) was studied. The IED-M required a minimum number of aggressive acts (2 times/wk for 1 mo) and the events must be spontaneous, excessive, and have associated anguish. A pilot study was performed to evaluate the validity of the IED-M in detecting IED in children. Olvera et al provided preliminary data that the IED-M is useful for detecting IED in teenagers.

**EPIEMIOLOGY**

As formulated in the DSM-IV-TR, IED is probably a rare disorder; however, recent data have indicated that this may not be true. In a chart review of 830 patients in 1983, only 1.1% were found to meet DSM-III criteria for IED. In a second report of 433 aggressive participants, 1.8% qualified for a diagnosis of IED by DSM-III standards. A 2005 study of 1300 patients seeking mental health care found that 6.3% met DSM-IV criteria for lifetime IED and 3.1% met criteria for a current diagnosis of IED. A face-to-face household survey of 9282 individuals found a lifetime and 12-month incidence of IED of 7.3% and 3.9%, respectively.

Most studies indicate onset of IED in adolescence. McElroy et al found an average age of onset of 14 years, with the disease lasting an average of 20 years. Seventy-four percent of the participants were male. Kessler et al also found the average disease onset of age 14 years as well as an average of 43 attacks over an individual’s life with an average cost of $1359 for damaged objects per lifetime. In the study, injuries related to the disorder occurred 180 times for every 100 lifetime cases. Risk factors included male sex, young age, lower level of education, being married, employment, and having decreased revenue within the home. Another study found that IED showed a linear pattern of occurrence from young to old and lower to higher education. Individuals who completed a college degree or beyond were 2 times less likely to meet criteria for IED than those who had a high school diploma and/or some college. Further, high school graduates were 2 times less likely to meet criteria for IED as those who did not graduate high school. IED was less common in whites as compared with nonwhites.

**ETIOLOGY AND PATHOPHYSIOLOGY**

At one time, theories regarding impulsive aggression included possession by spirits, humeral imbalances, and moral weakness. As psychiatry advanced, so did its theories on impulsive aggression. In the latter part of the 19th century, 2 main theories evolved: (1) impulsive aggression was, at least in part, due to events experienced in youth and (2) impulsive aggression was the result of gender differences in proactive and reactive aggression.

In studies involving rhesus monkeys, researchers found that disrupting early attachment to parental figures was a risk factor for becoming aggressive at improper times. In a human study that measured differences in brain chemistry and makeup.

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**Table 1. DSM-IV-TR Diagnostic 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 (eg, antisocial personality disorder, borderline personality disorder, psychotic disorder, manic episode, conduct disorder, attention-deficit/hyperactivity disorder) and are not due to the direct physiologic effects of a substance (eg, a drug of abuse, a medication) or a general medical condition (eg, head trauma, Alzheimer’s disease) |

Table 2. Psychiatric Disorders That Present with Impulsive Aggression

<table>
<thead>
<tr>
<th>Mental Disorder</th>
<th>Features</th>
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<td>Antisocial personality disorder</td>
<td>Pervasive pattern of disregard for and violation of the rights of others; symptoms may include irritability and aggressiveness (eg, repeated physical fights and assaults)</td>
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<td>Borderline personality disorder</td>
<td>Pervasive pattern of instability of relationships, self-image, and affects, and marked impulsivity; symptoms may include inappropriate, intense anger or difficulty controlling anger (eg, frequent displays of temper, constant anger, recurrent physical fights)</td>
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<td>Conduct disorder</td>
<td>Repetitive and persistent pattern of behavior in which basic rights of others or societal norms and rules are violated; symptoms may include aggression towards people and animals (eg, bullies/threatens others, initiates physical fights) or destruction of property</td>
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<td>Dementia with behavioral disturbance</td>
<td>Aggression is a common behavioral symptom of dementia. Patients with dementia can become combative with staff or loved ones who attempt to help them with their personal care</td>
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<tr>
<td>Personality change caused by a general medical condition, aggressive type 6</td>
<td>Aggression can be caused by multiple neurologic conditions</td>
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<tr>
<td>Posttraumatic stress disorder (PTSD)</td>
<td>Although aggression is not included in the diagnostic criteria for PTSD, it is a recognized characteristic</td>
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Impulsive aggression. It has been suggested that decreased serotonin in CSF concentrations can lead to the inability to constrain the impulse that causes “offensive aggression.” This is supported by studies in which monkeys with decreased CSF serotonin exhibit “risky” behavior. Adolescent male rhesus macaques with low CSF concentrations showed high levels of aggression and were at greater risk of death at a young age due to aggression. In rodent studies, there was a noted increase in aggression with decreased brain serotonin as well as increased killing among the rodents with low serotonin. The more aggressive impulses were also seen when serotonergic neurons were depleted. However, when serotonin in the brain was replaced, aggression remitted. In a study comparing murderers with suicide attempters, suicide attempters had decreased levels of CSF 5-HIAA, whereas the murderers did not. However, murderers who killed their sexual partners had extreme low levels of CSF 5-HIAA. The authors assumed the murders were performed during times of high affective response and concluded that serotonin abnormalities are seen in violence “in states of emotional turmoil.” Aggression in adults and adolescents after puberty has been seen in individuals with increased testosterone levels.

Specific areas of the brain, including the prefrontal cortex and the amygdala, have been suspected to be associated with impulsive aggression. Increased aggressive behavior has been seen in individuals with lesions in the frontal or temporal lobes. Impulsivity can be seen in damage to the frontal lobe. In a study using functional magnetic resonance imaging to examine response inhibition, more impulsive individuals activated higher order association areas when inhibiting a prepotent response. Other studies have shown that areas of the prefrontal cortex can be involved in impulsive aggression, and brain positron emission tomography has demonstrated a decreased glucose metabolism in prefrontal and frontal cortex in these patients.

Differential Diagnosis

A medical work-up should be performed before a diagnosis of IED is given. If the patient has a history of memory loss, head trauma, or seizures, a neurology consult may be considered. Imaging studies and electroencephalography (EEG) may also be helpful. There are many neurologic disorders that can cause aggressiveness, including brain abscesses, dementia, partial complex seizures, encephalitis, frontal focal lesions, and cerebrovascular accident. In these neurologic conditions, personality change due to a general medical condition, aggressive type is the correct diagnosis.

In patients with IED, physical examination may reveal nonspecific soft neurologic signs, such as minor difficulties in hand-eye coordination or small reflex asymmetries. There may also be hypersensitivity to sensory stimuli or abnormalities on EEG. In individuals with anger that occurs suddenly, slowing may be seen throughout the EEG.

IED is a diagnosis of exclusion, and, as such, other psychiatric diagnoses must first be ruled out (Table 2). Because many psychiatric disorders can present with a history of impulsive aggression, distinguishing IED from other psychiatric disorders can be difficult. Antisocial personality disorder, borderline personality disorder, conduct disorder, dementia with behavioral disturbance, oppositional

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defiant disorder, personality change caused by a general medical condition, aggressive type, and posttraumatic stress disorder (PTSD) all involve aggression. A diagnosis of IED should be considered only after other diagnoses for impulsive aggression have been invalidated.

When distinguishing IED from personality disorders, it is often helpful to consider baseline behavior. Aggressive behavior demonstrated on a normal daily basis is in stark contrast to the discrete episodes of impulsive aggressiveness seen in IED. In children, symptoms of bipolar disorder and IED can be similar.

The inappropriate expression of anger is a key feature in borderline personality disorder. Patients with borderline personality disorder or antisocial personality disorder often describe a history of lifetime of continuous impulsive aggression instead of discrete episodes of aggression.

Aggression (physical, verbal, or sexual) is commonly seen in older individuals with dementia. The physical aggression seen in this disease process is often the prompt that leads to nursing home placement. Aggression may also be seen if individuals are under the influence or withdrawing from a substance. IED would not be diagnosed in either circumstance.

A study addressing anger and aggression in outpatient psychiatric patients found that generalized anxiety disorder and drug abuse/dependence were linked to higher rates of aggression. IED, bipolar I disorder, and PTSD were most likely to be linked with current aggressive behavior. Although aggression is not officially recognized as a characteristic of PTSD, new evidence is emerging to support that aggression does occur in PTSD. Fifty couples in which the male was a Vietnam veteran were questioned. All of the men exhibited PTSD symptoms. The survey found that 100% of these men participated in psychological aggression against their mate, 92% engaged in verbal aggression, and 34% had 1 or more episodes of physical aggression.

Another type of aggression, anger attacks, may be seen in depressed patients and usually occur when a person feels emotionally trapped and experiences outbursts of anger. These attacks may include irritability, autonomic symptoms, and exaggerated reaction to a small irritant with rage. Three studies indicated that in patients with major depression, anger attacks were seen between 38% and 44% of the time. Studies indicate that 30% to 40% of patients with any type of depression have anger attacks.

**COMORBIDITY**

Studies have indicated that most individuals with IED have a least 1 other lifetime DSM-IV diagnosis (Table 3). In a report of 27 cases of IED, 26 (96%) met requirements for at least 1 other DSM-IV Axis I diagnosis, and 19 (70%) patients met criteria for 3 or more diagnoses. Of the 27 patients, 25 (93%) met criteria for a mood disorder during their lifetime, and 14 (52%) met lifetime criteria for bipolar disorder. Thirteen patients were diagnosed with a type of anxiety disorder, 13 were diagnosed with a substance abuse/dependence disorder, 6 were diagnosed with eating disorders, and 12 had other impulse-control disorders. Five patients reported a diagnosis of attention-deficit/hyperactivity disorder as a child. Some participants with mood and substance use disorders reported changes in their IED symptoms with changes in mood or substance use. Six participants noted worsening IED symptoms during depression, while 5 noted a worsening of IED during manic attacks. Of the 7 women included in the study, 5 noted that IED worsened during their premenstrual period. All individuals with substance use disorders reported changes in their IED symptoms with substance use; 7 patients noted an increase in IED symptoms with alcohol use whereas 2 noted a decrease, and 5 individuals stated that marijuana decreased their IED symptoms. Incidence of headache in the sample was high, with 12 of the participants reporting migraine headaches.

Coccaro et al studied 1300 patients requesting outpatient treatment and found that in addition to meeting criteria for IED, 75.6% also met criteria for a lifetime mood disorder, 32.7% met criteria for personality...
disorders, 59.8% met criteria for a substance use disorder, and 78% met criteria for anxiety disorders. The National Comorbidity Survey Replication found that 81.8% of individuals with lifetime broad IED also had at least 1 or more other lifetime DSM-IV diagnosis. In this study, the odds ratios of IED with impulse-control and substance use disorders were not higher than those with mood and anxiety disorders. Based on these data, the author proposed that IED may be as much related to affective instability and dysregulation as to problems with impulse control. This study also found that IED had an earlier age of onset than most comorbidities, suggesting that IED could be a “risk factor” for diseases such as major depression, generalized anxiety disorder, panic disorder, and substance abuse disorders. However, there are no published data to confirm this suspicion. There is also some speculation that IED is also associated with bipolar disorder, as many individuals who meet criteria for IED also have a lifetime diagnosis of bipolar disorder.

**TREATMENT**

There are few studies evaluating treatment for IED. Further, the U.S. Food and Drug Administration has not approved any medications for the treatment of aggression. The National Comorbidity Survey Replication indicated that individuals who sought treatment for IED often waited until well after their first episode, and when they did seek treatment, it was commonly for another comorbid condition. Many people with IED will eventually seek mental health treatment but not for their anger episodes. It could be that many patients may not feel that anger is a reason to seek psychiatric treatment. One study found that only 20% of individuals with IED who sought treatment described IED as the reason for mental health treatment.

**PHARMACOLOGIC THERAPY**

Although there is a paucity of studies defining treatment for IED, McElroy published an algorithm for treating angry or combative individuals (Figure). According to this algorithm, patients with unipolar depression should be started on a serotonin reuptake inhibitor, other antidepressants, or lamotrigine, whereas those with bipolar depression with a history of mania or mixed episodes should be treated with a mood stabilizer, antipsychotics, other antiepileptics, or antiandrogens. If there is no affective component, it should be determined whether the individual presented with compulsive or impulsive primary symptomatology. If the patient complains of compulsivity, selective serotonin reuptake inhibitors (SSRIs) or other serotonin agents are used. If the patient complains of impulsivity, SSRIs, other antidepressants, mood stabilizers, antiepileptics, β blockers, stimulants, or antiandrogens should be prescribed. In a study of 27 patients with IED, 20 received treatment with either a mood stabilizer or SSRI. At least a moderate response to medication was described by 60% of the individuals.

Lithium has been found to be effective in decreasing aggression in several studies in differing patient populations. In a study involving 66 young nonpsychotic adult and adolescent prisoners (age range, 16–24 yr), lithium was superior to placebo in demonstrating reduced aggressive episodes. In a 6-week, double-blind, placebo-controlled study of adolescents with conduct disorder, patients taking lithium demonstrated reduced aggression compared with those taking placebo.

Improvements in aggression have been seen in adolescent males with the addition of valproic acid. In a placebo-crossover, double-blind, parallel-group study of 20 teens diagnosed with oppositional defiant disorder or conduct disorder and problematic temper and mood liability, valproic acid was superior to placebo in demonstrating reduced aggression.

Several studies have shown that carbamazepine lessens aggression in multiple psychiatric disorders. Two open studies performed by Mattes and Mattes et al found that carbamazepine lessened aggression in rageful patients. Both studies included patients with multiple diagnoses; 12 of 28 and 19 of 34 patients, respectively, had been diagnosed with IED. In a randomized, double-blind study by Neppe, aggression was 1.5 times less common when treated with carbamazepine compared with placebo. These individuals were chronic psychiatric hospitalized inpatients who did not have epilepsy but had abnormal temporal lobe findings on EEG. Phenytoin has also been shown to decrease impulse aggression. In a double-blind, placebo-controlled, crossover study performed on 60 inmates, the inmates with impulsive aggression had reductions in aggressive behavior.

In a study of impulsive aggression in 40 patients with a personality disorder, patients treated with fluoxetine showed a significant reduction in aggressive symptoms compared with the placebo group, as measured by the Overt Aggression Scale Modified for Outpatients. All 40 participants in this study were found to fulfill IED research criteria. SSRIs may take approximately 3 months to reach full benefit in patients with IED; thus, a sufficient trial of an SSRI should include at least 3 months. Symptoms also tend to reappear shortly after the medication is discontinued.
β Blockers may also be used to treat aggression in some patients, but they have worrisome side effects, such as bradycardia, dizziness, and hypotension, and the appropriate dose is difficult to determine.\cite{15,35} Studies evaluating pindolol in brain damaged patients showed a lessening of aggression in these patients.\cite{5} Another study demonstrated a lessening of aggression in adolescents who were given α2 agonists.\cite{36} However, their use in this setting has been questioned due to reports of sudden death in young patients taking α2 agonists with other drugs. The side effects include worsening depression, sedation, and decreased blood pressure.\cite{5}

Recent studies have shown atypical antipsychotics to be effective in treating aggression.\cite{37,38} Atypical antipsychotics have a preferred side effect profile compared with typical antipsychotics.\cite{5}

**NONPHARMACOLOGIC THERAPY**

Cognitive behavioral therapy has been shown to decrease anger and aggression in individuals with anger problems. These trials were not specific to IED patients; thus, more studies are needed to confirm the effectiveness of cognitive behavioral therapy in patients with IED.\cite{15} In a small sample (n = 4) of patients who received insight-oriented or supportive psychotherapy when exhibiting IED signs, 3 of 4 found that it was useful for constraining their impulsive aggression. All 4 patients receiving family, couples, or group therapy reported no reduction in aggressive behavior with therapy.\cite{8}

**CONCLUSION**

IED is characterized by impulsive aggression occurring in discrete episodes. Impulsive aggression is seen in multiple conditions; thus, IED is a diagnosis of exclusion, and other conditions in which aggression is seen should first be ruled out before IED is diagnosed. IED also occurs in association with other psychiatric disorders, adding to the difficulty in making an appropriate diagnosis. Although the etiology is uncertain, IED has been hypothesized to originate as a result of either childhood events or alterations in brain chemistry, particularly alterations in serotonin.\cite{3} Age of onset is
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adolescence, and risk factors include male sex, young age, being married, a decreased household income, and a high degree of social impairment. Studies evaluating IED are sparse, and studies evaluating treatments for IED are even more so. Currently, there are no drugs approved for the treatment of aggression; however, studies have demonstrated decreased aggression in certain populations with the use of pharmacologic agents, such as lithium, atypical antipsychotics, valproic acid, phenytoin, SSRIs, and β blockers, and psychotherapy.

SUMMARY POINTS

- Recent studies have indicated that IED is much more prevalent than previously thought; a recent study of 9282 individuals found an incidence of 7.3% for lifetime diagnosis of IED and 3.9% 12-month incidence rate.
- Diagnosis of IED can be difficult due to vagueness of the diagnostic criteria and the frequency of impulsive aggression seen in other illnesses.
- When diagnosing IED, it is important to remember that the episodes of rage are short and substantially out of proportion to the stressor causing the event, and the episodes result in property damage or assault of individuals.
- IED is a diagnosis of exclusion; thus, all other causes of rage and outbursts must be excluded before giving this diagnosis. Other diagnoses that can mimic IED include neurologic disorders, antisocial personality disorder, borderline personality disorder, conduct disorder, dementia with behavioral disturbance, oppositional defiant disorder, and PTSD.
- Aggression of different forms is very common when patients are withdrawing or under the influence of different substances. These individuals should not be diagnosed with IED.
- Patients with IED are at risk for high impairment in multiple aspects of their life. Many report difficulties psychosocially, and individuals with IED often have difficulties with significant relationships throughout their life.
- The intensity of IED tends to lessen as the patient becomes older.
- IED-related behavior is not the same as well-planned criminal behavior. If the behavior is premeditated, individuals should not be given a diagnosis of IED.
- Although the average age of onset of IED appears to be in adolescence, most patients do not seek treatment until they are much older. The reason for seeking treatment is most often another psychiatric condition they have comorbidly.
- Most patients with IED have at least 1 other lifetime DSM-IV diagnosis. It is common for individuals with this disorder to met criteria for 3 or more diagnoses. Mood and anxiety disorders are often seen comorbidly in patients with IED.
- Risk factors for IED include male sex, young age, low level of education, marriage, employment, and having decreased revenue in the home.
- IED is thought to arise as a result of experiences from youth and differences in brain chemistry. Early disruption of attachment to a primary caregiver or aggressive parenting has been shown to be risk factors for aggressive behaviors as adults. A decreased level of serotonin activity in the CSF has been seen in aggressive individuals.
- Studies have indicated that certain areas of the brain, including the prefrontal cortex and amygdala, are involved in aggression. Individuals with lesions in the frontal or temporal lobe have been shown to have increased aggression.
- According to McElroy, violent individuals with unipolar depression should be started on a serotonin reuptake inhibitor, another antidepressant, or lamotrigine. Individuals with bipolar depression and a history of mania should be treated with a mood stabilizer, antipsychotics, other antiepileptics, or antiandrogens.
- If no affective component is present, patients should be evaluated for compulsive verses impulsive primary symptomatology. If the patient has compulsive symptoms, SSRIs or other serotonin agents are indicated. If the patient has impulsivity symptoms, SSRIs, other antidepressants, mood stabilizers, antiepileptics, β blockers, stimulants, or antiandrogens are indicated.
- In certain populations, studies have indicated that pharmacologic treatments, such as lithium, valproic acid, carbamazepine, phenytoin, fluoxetine, or atypical antipsychotics, are more effective than placebo in treating aggression.
- Nonpharmacologic therapy, such as cognitive behavioral therapy, can help decrease anger episodes in patients with anger problems. A small study indicated that insight-oriented and supportive psychotherapy was helpful in controlling aggression in some patients when exhibiting signs of IED.
REFERENCES


