Intermittent Explosive Disorder: Clinical Aspects

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History of Psychiatric Attention to Intermittent Explosive Disorder

Intermittent explosive disorder (IED) is a psychiatric diagnosis applied to individuals who repeatedly engage in acts of impulsive aggression. The diagnosis of IED has been a part of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) only since the introduction of the third edition (DSM-III) in 1980. However, the construct of a "disorder of impulsive aggression" has been a part of the DSM since its inception in 1956.

In the first edition (DSM-I), 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 construct evolved into "explosive personality" in the second edition (DSM-II). Patients with "explosive personality" were characterized as being "aggressive individuals" who display "intermittently violent behavior" and are "generally excitable, aggressive, and over-responsive 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 regarding which behaviors would satisfy the criteria for severity, frequency, or time frame) 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). Because individuals with recurrent, problematic, impulsive aggression are also generally impulsive and aggressive between more severe outbursts, this exclusion ruled out the vast majority (i.e., about 80%) of individuals who now would be diagnosed with IED (Felthous et al. 1991).

Current IED Criteria Sets

With the introduction of the fourth edition (DSM-IV), the earlier exclusionary "C" criteria that excluded individuals with chronic aggression problems (effectively excluding most subjects now considered IED) was removed. This had the net effect of allowing for more empirical work to take place. The DSM-IV still lacked objective criteria for the intensity, frequency, and nature of aggressive acts to meet criteria for IED (see Table 20.1).

The World Health Organization's (WHO) diagnostic manual, the *International Classification of Mental and Behavioral Disorders* (ICD-10) (World Health Organization 1992), has no IED diagnosis. The closest approximation to IED in the ICD-10 is the diagnosis of "other habit and impulse disorders," which is broadly defined as persistently maladaptive behavior in which there is a "failure to resist impulses to carry out the behavior." In addition, the

Table 20.1 DSM-IV 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 a result of the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., head trauma, dementia of the Alzheimer's type).

behavior must involve "a prodromal period of tension with a feeling of release at the time of the act" that is not secondary to another psychiatric condition (World Health Organization 1992).

Noting the limitations of the DSM-IV (and ICD-10) criteria for IED, Coccaro and colleagues developed an alternative criteria set that integrated their research findings with the DSM conceptualizations of IED (Coccaro 2003; Coccaro et al. 1998). These "integrated research" criteria for IED (IED-IR), differed from DSM-IV IED criteria on four key points.

First, the IED-IR criteria clearly operationalized the severity and frequency of aggressive behavior required for the diagnosis. Using the IED-IR criteria, individuals could be diagnosed by the presence of frequent low-intensity aggression (e.g., arguments occurring on average twice weekly) and/or of less frequent but higher-intensity aggressive behavior (e.g., physical assault or destruction of property three times in a year). The inclusion of verbal aggression within the IED-IR construct reflected data showing both that frequent verbal aggression occurred in over 85% of subjects with physical aggression and that subjects with frequent verbal aggression in the absence of more severe assaultive acts show the same core deficits and impairment as assaultive subjects (Coccaro 2003; Coccaro et al. 1998; McCloskey et al. 2008a). Furthermore, both groups manifest similar serotonergic deficits and an antiaggressive response to serotonin reuptake inhibitors (Coccaro and Kavoussi 1997; Salzman et al. 1995).

Second, the IED-IR criteria explicitly required the aggressive behavior to be impulsive in nature. This decision was also informed by research showing that psychosocial (Dodge, Pettit, and Bates 1994), biological (Linnoila et al. 1983; Virkkunen et al. 1994) and treatment response data (Barratt et al.1997; Sheard et al. 1976) differentiated between "impulsive" and "premeditated" aggression.

Third, the IED-IR criteria explicitly required the presence of subjective distress (i.e., in the individual) and/or social or occupational dysfunction in order to clearly link distress/dysfunction to aggressive behavior.

Fourth, the IED-IR criteria allowed subjects with borderline and/or antisocial personality disorder (BPD/AsPD) to receive a comorbid IED diagnosis (i.e., if they otherwise meet the IED-IR criteria). This decision stemmed from the finding that IED subjects with and without BPD/AsPD are similarly aggressive, and both IED groups are much more aggressive, than non-IED subjects with BPD/AsPD. In other words, high levels of aggression were always associated with the presence of IED but not necessarily the presence of BPD/AsPD (see the subsection on "Comorbidity"). These research criteria for IED (Table 20.2) have been used in studies of IED in several sites in the United States (Frankle 2005; Goveas, Csernansky, and Coccaro 2004; Hollander et al. 2003; New et al. 2002, 2004; Siever et al. 1999). Moreover, some suggested changes have been adopted in the text revision edition of the DSM-IV.

Table 20.2 Research criteria for IED: IED-IR

- A. Recurrent incidents of aggression manifest as either:
- A1. Verbal or physical aggression toward other people, animals, or property occurring twice weekly on average for 1 month
- A2. Three episodes involving physical assault against other people or destruction of property over a 1-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 (i.e., it 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 disease); or the direct physiological effects of a substance.

Differential Diagnosis

The cardinal symptom of IED is repeated acts of impulsive (affective) aggression that are not better accounted for by another psychiatric disorder, medical condition, or substance. This is true of both DSM and integrated research criteria sets. However, many psychiatric disorders (e.g., mood disorders, personality disorders) and some substances (e.g., alcohol) are both associated with increased aggression and comorbid with IED, making differential diagnosis difficult. In many of these situations, a determination of whether IED is present can be made by assessing the temporal relationship between the disorder, the substance use, and the aggressive behavior.

Bipolar disorder, and to a lesser extent unipolar depression, have been linked to increased agitation and aggressive behavior in some individuals (Fava and Rosenbaum 1999; Swann 1999), but for these individuals the pathological aggressiveness is limited to the manic and/or depressive episodes. For individuals with IED, even if a mood disorder exists, heightened levels of aggressive behavior persist during otherwise euthymic periods.

Similarly, alcohol and other substance use disorders facilitate aggression (Wells, Graham, and West 2000). If individuals abusing these substances display aggressive behavior that would otherwise meet criteria for IED but that only occurs during periods of acute intoxication and/or withdrawal, then they would not receive an IED diagnosis. However, if the individual also engaged in sufficient aggressive behavior when not intoxicated or going through withdrawal, then IED would be diagnosed.

For chronic disorders, differential diagnosis is considerably more difficult. Individuals with IED are more likely to have experienced past traumatic events. They also tend to be hypervigilant and perseverate on perceived injustices; however, they do not share the reexperiencing of symptoms (i.e., flashbacks, highly distressing intrusive thoughts) that occur with posttraumatic stress disorder (PTSD). If a person appears to meet criteria for both PTSD and IED, the clinician should assess whether the level of aggression met IED criteria prior to the trauma. The onset of IED is typically in early adolescence. If the trauma occurred later than adolescence and the aggressive behavior began around the time of other PTSD symptoms, then an additional diagnosis of IED would not be warranted.

DSM-IV criteria for antisocial (AsPD) and borderline (BPD) personality disorders include anger and aggression (though these are not required symptoms as they are for IED). Because the symptoms of AsPD, BPD, and IED all develop in adolescence, determining whether the aggressive behavior in AsPD or BPD is associated with the personality disorder or IED is difficult. Unlike IED patients, some individuals with AsPD primarily engage

	Controls		Non-IED Subject		IED
Subjects' Sample Site	Healthy Controls	Personality Dx without IED	BPD/AsPD without IED	IED without BPD/AsPD	IED with BPD/AsPD
Philadelphia ($n = 437$) Chicago ($n = 352$)	4.9 ± 4.2^a 5.3 ± 3.8^a	7.9 ± 5.2^{b} 11.5 ± 5.9^{b}	$10.2 \pm 4.9^b 10.3 \pm 5.2^b$	16.4 ± 5.6^{c} 17.7 ± 4.4^{c}	18.9 ± 5.0^{c} 19.5 ± 3.8^{c}

Table 20.3 LHA aggression scores (mean \pm SD): Relevance to IED not BPD/AsPD

in aggression that is motivated by tangible rewards other than revenge (e.g., mugging a person to steal their money). For these individuals, a second diagnosis of IED would not be warranted.

However, for the majority of AsPD and BPD patients, the aggressive behavior is predominately in response to angry feelings. How to diagnose these individuals is a point of variance between the DSM-IV and Research IED criteria sets. While proponents of both IED criteria sets posit that aggressive behavior should "count" toward the diagnosis of AsPD and/or BPD, the DSM-IV criteria allow for an IED diagnosis *only* if the aggressive behavior is not better explained by AsPD and/or BPD. The text of DSM-IV does not explain how to make this determination. However, data suggest that individuals with AsPD and/or BPD who do not otherwise meet criteria for IED are not more aggressive than other patients with non-AsPD/BPD personality disorders (see Table 20.3). Accordingly, the mere presence of AsPD/BPD does not explain the presence of aggressiveness in the individual, and therefore IED should be diagnosed in AsPD/BPD individuals when the criteria for IED are met. This is why the IED-IR criteria allow IED to be comorbid with AsPD and/or BPD.

Clinical Picture and Course of Illness

Prevalence

Since its initial inclusion in the DSM, IED has been described as "rare" (American Psychiatric Association 1994). However, this designation was based on very limited empirical research. Two recently published epidemiological studies found that approximately 4%–6% of individuals met lifetime criteria for IED, depending on the criteria set used (Coccaro et al. 2004; Kessler et al. 2006). One-month and 1-year point prevalences of IED in these studies were reported as 2.0% (Coccaro et al. 2004) and 2.7% (Kessler et al. 2006), respectively. If so, 16.2 million Americans will have IED during their lifetimes and as many as 10.5 million in any year and 6 million in any month. Prevalence was not associated with race in these studies. This result is consistent with a separate epidemiological survey of 2,554 Latinos that found a lifetime IED prevalence of 5.8% (Ortega, Canino, and Alegria 2008). Furthermore, a study of 4,725 respondents in the Ukraine found comparable rates of lifetime IED (4.2%), suggesting that a lifetime prevalence of IED of 4%–6% is not limited to American samples (Bromet et al. 2005).

Symptom Presentation

Aggressive outbursts in IED have a rapid onset (McElroy et al. 1998), often without a recognizable prodromal period (Felthous et al. 1991; Mattes 1990). Episodes are short-lived—less than 30 minutes (McElroy et al. 1998) — and involve verbal assault, destructive and

a = p < .05 from all groups.

b = p < .05 from HC & IED subjects.

c = p < .05 from HC & non-IED subjects.

BPD/AsPD = borderline personality disorder and/or antisocial personality disorder.

LHA = Lifetime history of aggression.

IED = Intermittent explosive disorder.

nondestructive property assault, or physical assault (Mattes 1990; McElroy et al. 1998). Aggressive outbursts most commonly occur in response to a minor provocation by a close intimate or associate (Felthous et al. 1991; McElroy et al. 1998), and IED subjects may have less severe episodes of verbal and nondestructive property assault in between more severe episodes (Coccaro 2003; McElroy et al. 1998). Episodes are associated with substantial distress, impairment in social functioning, occupational difficulty, and legal or financial problems (Mattes 1990; McElroy et al. 1998).

In a recent community sample study of more than 9,200 individuals, subjects meeting current IED criteria (defined as three high-severity episodes in the current year) had engaged in direct interpersonal aggression (67.8%), threatened interpersonal aggression (20.9%), and aggression against objects (11.4%). These subjects reported engaging in 27.8 (SD = 4.1) high-severity aggressive acts during their worst year, with two to three lifetime aggressive outbursts requiring medical attention. The mean dollar value of property damage due to lifetime IED aggressive outbursts was \$1,603 (SD = \$135) (Kessler et al. 2006).

Quality of Life

High levels of hostility and aggression negatively impact quality of life across several dimensions, including interpersonal relationships (Laurent, Kim, and Capaldi 2007; Lawrence and Bradbury 2007), sleep quality (Ireland and Culpin 2006), job satisfaction (Judge, Scott, and Ilies 2006), and health (Miller et al. 1995; Vahtera et al. 1997). Similarly, the limited data suggest that individuals with IED have more health problems (McCloskey et al., submitted), are more impaired in terms of overall functioning, and are less happy than healthy volunteers or psychiatric controls (McCloskey et al. 2006, 2008). Notably, their quality of life improves after successful treatment (McCloskey et al. 2008b). There is a dearth of data on the impact of IED on the quality of life of family members. However, numerous studies have linked witnessing and experiencing aggression in childhood with adverse adult consequences, including intergenerational transmission of aggression (Conger et al. 2003).

Age of Onset, Gender, and SES

Intermittent explosive disorder begins 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 (Coccaro et al. 2004; Coccaro, Posternak, and Zimmerman 2005; Kessler et al. 2006). In one study, the age of onset occurred at a significantly earlier time in males (Coccaro, Posternak, and Zimmerman 2005). The average duration of symptomatic IED ranges from 12 years to an adult's complete lifetime (Coccaro et al. 2004; Kessler et al. 2006; McElroy et al. 1998). Although IED is common in males (Coccaro et al. 1998; Mattes 1990; McElroy et al. 1998), recent data suggest that IED occurs equally among men and women (Coccaro et al. 2004; Coccaro, Posternak, and Zimmerman 2005; Kessler et al. 2005, 2006). In a large epidemiological survey, sociodemographic variables (e.g., sex, age, race, education, marital status, occupational status, family income) did not differ across IED statuses (Kessler et al. 2006).

Comorbidity

Available data suggest that IED is a chronic disorder whose onset *precedes* other comorbid Axis I disorders (Coccaro, Posternak, and Zimmerman 2005; Kessler et al. 2006). If so, it is unlikely that IED evolves into another disorder. It is more likely that IED promotes the development of other disorders by leading to divorce, financial difficulties, and stressful life experiences that promote their onset later in adulthood (Kessler et al. 2006). In clinical samples, IED is highly comorbid with a variety of Axis I disorders, such as mood disorders, anxiety disorders, and alcohol and other substance use disorders (Coccaro, Posternak, and Zimmerman 2005). In community samples, however, the odds ratios for a relationship

between current IED and such disorders were significant (p < .05) only for generalized anxiety disorder (OR = 2.1; 95% CI: 1.3–3.2), alcohol abuse (OR = 2.6; 95% CI: 1.7–4.2), and any substance use disorder (OR = 2.4; 95% CI: 1.5–3.8). Again, the vast majority of subjects reported that IED began at an earlier age than these comorbid conditions (Coccaro, Posternak, and Zimmerman 2005; Kessler et al. 2006).

For Axis II disorders, only subjects with borderline (BPD) and antisocial (AsPD) personality disorders are more highly represented among IED subjects compared with non-IED ones (Coccaro et al. 1998). This comorbidity is not due to individuals with BPD and/or AsPD in general having high levels of aggression and therefore IED. Data (Table 20.3) indicate that aggression levels among BPD/AsPD subjects with and without IED are the same and that levels of aggression in non-IED subjects are significantly less than those in IED subjects regardless of the presence or absence of BPD/AsPD. Accordingly, the key difference between IED subjects with and without BPD/AsPD is level of aggression, not the presence or absence of BPD and/or AsPD. In addition, while 40%–50% of IED subjects in these two samples had BPD/AsPD, only about 25% of BPD/AsPD individuals in the community meet criteria for IED (Coccaro et al. 2004).

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 the IED relatives compared with the control relatives (0.26 vs. 0.08, p < .01) (Coccaro 2003). 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 attempts, major depression, alcoholism, drug use disorder) nor by increases in morbid risk of other non-IED disorders in the relatives (e.g., major depression, alcoholism, drug use disorders, anxiety disorder, or any other disorder). Accordingly, familial aggregation of IED is not the result of 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 finding supports research showing that socially aberrant aggressive behavior reflects a substantial degree of genetic influence (Bergeman and Seroczynski 1998).

Biology

Laboratory studies clearly show a biobehavioral relationship between aggression and selected brain chemicals (e.g., serotonin) (Coccaro and Siever 2002), but studies in IED have been conducted only over the past few years. Published data suggest that IED subjects have altered serotonin function compared with non-IED subjects or healthy controls (Goveas, Csernansky, and Coccaro 2004; New et al. 2002, 2004). Reports of other studies supporting the IED-serotonin link are in preparation by the author (EFC). They demonstrate a reduction in prolactin responses to d-fenfluramine challenge and a difference in platelet 5-HT transporter numbers (measured via H³-paroxetine binding) in IED subjects compared with non-IED subjects or healthy controls. These findings are supported by imaging studies. Two fluorodeoxyglucose (FDG) PET studies found low FDG utilization after d,l-fenfluramine challenge in frontal cortex areas (Siever et al. 1999) and low FDG utilization after m-CPP challenge in the anterior cingulate in IED subjects compared with healthy controls (New et al. 2002). A third, ligand binding study of the 5-HT transporter also reports reduced 5-HT transporter availability in the anterior cingulate in IED subjects versus controls (Frankle 2005). Finally, an fMRI study (Coccaro et al. 2007) demonstrated increased activation of the amygdala and reduced activation of the orbital medial prefrontal cortex, when viewing angry faces in IED subjects compared with healthy controls. This reduced prefrontal activation may be dependent on the level of emotional information processing (McCloskey et al., submitted).

Assessment of IED

There are no well-validated measures of IED. However, two measures have been developed by the authors: a brief questionnaire that could be used as a screening measure and a semistructured interview to more thoroughly diagnose the disorder.

The Intermittent Explosive Disorder Module (IED-M) is a 20–30 minute structured diagnostic interview developed to obtain systematic information sufficient to make research diagnoses of current and lifetime IED by both DSM-IV and integrated research criteria. The IED-M obtains quantitative information about lifetime and current frequencies of verbal aggression, aggression against property, and physical aggression. Contextual descriptive information about the three most serious episodes of each type of aggression during the 1-year period in which it occurred most frequently (e.g., "what was the provocation?" and "what were the consequences of this outburst?") provide information about the proportionality of the aggressive response. Additional phenomenological information about aggressive acts is also obtained, including but not limited to age of onset and offset of each type of aggression, the effects of the aggressive behaviors on relationships with family and friends, subjective level of distress, emotions and physical symptoms prior to and after an outburst, and frequency of substance use during aggressive outbursts. Preliminary psychometric data suggest that the IED has strong interrater reliability (k = .83) when used as part of a full diagnostic battery that includes structured clinical interviews for other Axis I and Axis II disorders. Construct validity for the measure comes from research showing that individuals identified as having IED using the IED-M were more aggressive than psychiatric controls on a behavioral aggression measure (McCloskey et al. 2006).

The Intermittent Explosive Disorder Diagnostic Questionnaire (IED-DQ) is a brief, seven-item, self-report measure of IED according to DSM-IV criteria and research criteria for IED. The IED-DQ contains items that assess aggression frequency, severity, resulting distress from aggressive behavior and exclusionary mental health or medical conditions. Results from our developmental studies using the IED-DQ indicate good psychometric properties (test–retest reliability, construct validity, strong concordance – kappa \sim 0.80), with the best estimated diagnoses of IED established via a clinical interview such as the IED-M. Sensitivity and specificity for the IED-DQ versus the IED-M were 0.86 and 0.91, respectively, for the DSM-IV IED and were 0.85 and 0.95 for the IED by research criteria (McCloskey et al., submitted).

Treatment of IED

Psychopharmacologic Treatment

Impulsive Aggression

Several psychopharmacologic agents appear to have effects on aggression. Classes of agents shown to have "antiaggressive" effects in double-blind, placebo-controlled trials involving individuals with "primary" aggression (i.e., not secondary to psychosis, severe mood disorder, or organic brain syndromes) include mood stabilizers such as lithium (Donovan et al. 2000; Sheard et al. 1976), 5-HT uptake inhibitors such as fluoxetine (Coccaro and Kavoussi 1997; Fava et al. 1993; Salzman et al. 1995), and anticonvulsants such as diphenhydantoin at 300 mg/day or carbamazepine (Barratt et al. 1997; Gardner and Cowdry 1986). While betablockers such as propanolol or nadolol (Ratey et al. 1992; Yudofsky, Silver, and Schneider 1987) have also been shown to reduce aggression, these agents have been tested exclusively in patient populations with "secondary" aggression (e.g., mental retardation, organic brain syndromes, etc.). Classes of agents that may have "proaggressive" effects include tricylic antidepressants such as amitriptyline (Soloff et al. 1986), benzodiazepines (Gardner and Cowdry 1985), and stimulant and hallucinatory drugs of abuse such as amphetamines,

cocaine, and phencyclidine (Volavka and Citrome 1998). Emerging evidence of differential psychopharmacology is of critical importance, and double-blind, placebo-controlled clinical trials suggest that antiaggressive efficacy is specific to *impulsive* rather than nonimpulsive aggression (Barratt et al. 1997; Sheard et al. 1976).

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Completed analysis of a double-blind, placebo-controlled trial of fluoxetine on impulsive aggressive behavior in 100 subjects with IED (by research criteria) demonstrates clear antiaggressive efficacy for fluoxetine versus a placebo (Coccaro et al. 2009). This study notes reduction in overt aggressive behavior as reported by subjects, subjective or objective anger or 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 a placebo. In contrast, compared with fluoxetine, the placebo was associated with a greater frequency of increased aggression, and increased magnitude of aggression, after randomization. While the trial results are positive, only 29% of IED subjects displayed no aggression at the end of the trial, indicating that while fluoxetine can reduce impulsive aggressive behavior, remission of IED symptoms may take more than the drug itself. A placebo-controlled study involving divalproex, titrated to a plasma level of 80–120 mg/day, reported a favorable effect on overt aggression, but only in IED subjects with comorbid Cluster B personality disorder (Hollander et al. 2003).

Psychotherapy

Anger Dyscontrol

Despite the prevalence and burden of IED, no published randomized clinical trials (RCTs) have examined the efficacy of psychosocial treatments for this disorder. The efficacy of psychosocial interventions for the related construct of anger dyscontrol is well documented. Five meta-analytic reviews of anger treatments (Beck and Fernandez 1998; Bowman-Edmondson and Cohen-Conger 1996; Del Vecchio and O'Leary 2004; DiGuiseppe and Tafrate 2003; Tafrate 1995) support the conclusion that cognitive-behavioral therapies (e.g., relaxation training, self-inoculation training, cognitive restructuring, and multicomponent treatments) evidence a moderate to large effect for anger and aggression at the end of treatment, with similar effects at follow-up.

Overall, treatment efficacy was not dependent on the specific cognitive-behavioral intervention used, though multicomponent treatments containing both cognitive and behavioral components were most often employed. Furthermore, one review (Del Vecchio and O'Leary 2004) suggested that multicomponent treatments may be most effective for aggressive behavior. The generalizability of this research to IED is limited in that the anger-treatment literature often fails to discriminate between anger problems with and without pathological aggression. Highly aggressive individuals may be more resistant to treatment.

A meta-analysis of treatment for interpersonal (domestic) violence found that psychosocial interventions had only "small" effects on reducing aggression (Babcock, Green, and Robie 2004). However, the generalizability of this finding is also limited because only a small portion of individuals with IED have a history of domestic violence. One study that compared IED and non-IED aggressive drivers, who received a brief (four 90-minute sessions) cognitive-behavioral program, found that CBT was more effective than self-monitoring overall, but IED subjects tended not to respond as well to treatment. This led the authors to suggest that IED individuals may benefit from longer, more intensive therapy (Galovski and Blanchard 2002).

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The authors recently completed an IED psychotherapy outcome study (n = 45) comparing the efficacy of a 12-week multicomponent CBT intervention presented in either group or

individual format to a wait-list control group. The treatment was modeled after the Cognitive Restructuring, Relaxation and Coping Skills Training (CRCST) treatment developed to treat anger (Deffenbacher and Mckay 2000) but was modified to serve as a more appropriate treatment for aggressive individuals (e.g., extend treatment from 8 to 12 sessions, include a time-out technique, and increase emphasis on aggression and relapse prevention). Aggression, anger, and associated symptoms were assessed at baseline, midtreatment, post-treatment, and 3-month follow-up. Both group and individual CRCST reduced aggression, anger, hostile thinking, and depressive symptoms, while improving anger control relative to wait-list participants. 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 (McCloskey et al. 2008b).

Other Issues Regarding Treatment of IED

No studies have examined the optimal 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 one month of discontinuing fluoxetine, patients with impulsive aggressive behavior experience 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 levels within 1 month of a switch to a placebo (Sheard et al. 1976). This is in contrast to our findings regarding the effects of CRCST, which continue at least 3 months after active treatment has ended (McCloskey et al., in press). This is probably because the treatment elements (relaxation training, cognitive restructuring, and coping skills training) have been incorporated into the individual's life and are still active. In contrast, once medication leaves the body, its effects on behavior end.

In addition, no published studies have investigated the effect of combining modalities of treatment. Examining our own data with fluoxetine and CRCST in IED subjects, we are struck by the observation that both modalities yield a similar magnitude of improvement in outcome measures (e.g., $\sim 30\%$ remission and $\sim 15\%$ partial remission from IED). Because these two modalities work through different mechanisms, we hypothesize that together they would be more effective than either is alone. Our clinical experience is consistent with this idea, but these data are anecdotal. Whether medication or CRCST should be first-line probably depends on the patient because some prefer medication (some individuals perceive this as easier) whereas others prefer psychotherapeutic treatment (some individuals wish to avoid medications). Severity of aggression also affects the choice of modality, and combining medication and CRCST could be a first-line treatment in cases of severe aggressive behavior.

Helpful resources for victims of intimate partner violence can be found in Chapter 22 of this volume.

References

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition. Washington, DC: American Psychiatric Association, 1994.

Babcock JC, Green CE, Robie C. Does batterers' treatment work? A meta-analytic review of domestic violence treatment. *Clin Psychol Rev* 23:1023–1053, 2004.

Barratt ES, Stanford MS, Felthous AR et al. The effects of phenytoin on impulsive and premeditated aggression: A controlled study. *J Clin Psychopharmacol* 17:341–349, 1997.

Beck R, Fernandez E. Cognitive-behavioral therapy in the treatment of anger. *Cognit Ther Res* 22:62–75, 1998.

Bergeman C, Seroczynski A. Genetic and environmental influences on aggression and impulsivity, in *Neurobiology and Clinical Views on Aggression and Impulsivity*. Edited by Maes M, Coccaro E. London: Wiley, 1998, pp. 63–80.

- Bowman-Edmondson C, Cohen-Conger J. A review of treatment efficacy for individuals with anger problems: Conceptual, assessment and methodological issues. *Clin Psychol Rev* 16:251–275, 1996.
- Bromet EJ, Gluzman SF, Paniotto VI et al. Epidemiology of psychiatric and alcohol disorders in Ukraine: Findings from the Ukraine World Mental Health survey. *Soc Psychiatry Psychiatr Epidemiol* 40:681–690, 2005.
- Coccaro E, Siever L. Pathophysiology and treatment of aggression, in *Neurosychopharmacology: The Fifth Generation of Progress*. Edited by Davis KL, Charney D, Coyle JT et al. Nashville, TN: American College of Neuropsychopharmacology, 2002, pp. 1709–1723.
- Coccaro EF. Intermittent Explosive Disorder. New York: Marcel Dekker, 2003.
- Coccaro EF, Kavoussi RJ. Fluoxetine and impulsive aggressive behavior in personality-disordered subjects. Arch Gen Psychiatry 54:1081–1088, 1997.
- Coccaro EF, Kavoussi RJ, Berman ME et al. Intermittent explosive disorder-revised: Development, reliability, and validity of research criteria. *Compr Psychiatry* 39:368–376, 1998.
- Coccaro EF, Lee R, Kavoussi RJ. A double-blind, placebo-controlled, trial of fluoxetine in impulsive aggressive patients with Intermittent Explosive Disorder. J Clin Psychiatry 70:653–662, 2009.
- Coccaro EF, McCloskey MS, Fitzgerald DA et al. Amygdala and orbitofrontal reactivity to social threat in individuals with impulsive aggression. *Biol Psychiatry* 62:168–178, 2007.
- Coccaro EF, Posternak MA, Zimmerman M. Prevalence and features of intermittent explosive disorder in a clinical setting. *J Clin Psychiatry* 66:1221–1227, 2005.
- Coccaro EF, Schmidt CA, Samuels JF et al. Lifetime and 1-month prevalence rates of intermittent explosive disorder in a community sample. *J Clin Psychiatry* 65:820–824, 2004.
- Conger RD, Neppl T, Kim K et al. Angry and aggressive behavior across three generations: A prospective, longitudinal study of parents and children. *J Abnorm Child Psychol* 31:143–160, 2003.
- Deffenbacher JL, Mckay M. Overcoming Situational and General Anger. Oakland, CA: New Harbinger Publications, 2000.
- Del Vecchio T, O'Leary KD. Effectiveness of anger treatments for specific anger problems: A metaanalytic review. *Clin Psychol Rev* 24:15–34, 2004.
- DiGuiseppe R, Tafrate RC. Anger treatment for adults: A meta-analytic review. Clin Psychol: Sci Pract 10:70–84, 2003.
- Dodge KA, Pettit GS, Bates JE. Socialization mediators of the relation between socioeconomic status and child conduct problems. *Child Dev* 65(2 spec no): 649–665, 1994.
- Donovan SJ, Stewart JW, Nunes EV et al. Divalproex treatment for youth with explosive temper and mood lability: A double-blind, placebo-controlled crossover design. *Am J Psychiatry* 157:818–820, 2000.
- Fava M, Rosenbaum JF. Anger attacks in patients with depression. *J Clin Psychiatry* 60 (suppl 15): 21–24, 1999.
- 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* 150:1158–1163, 1993.
- Felthous AR, Bryant SG, Wingerter CB et al. The diagnosis of intermittent explosive disorder in violent men. *Bull Am Acad Psychiatry Law* 19:71–79, 1991.
- Frankle WG, Lombardo I, New AS et al. Brain serotonin transporter distribution in subjects with impulsive aggressivity: A positron emission study with [11C]McN 5652. *Am J Psychiatry* 162:915–923, 2005.
- Galovski T, Blanchard EB. The effectiveness of a brief psychological intervention on court-referred and self-referred aggressive drivers. *Behav Res Ther* 40:1385–1402, 2002.
- Gardner DL, Cowdry RW. Alprazolam-induced dyscontrol in borderline personality disorder. Am J Psychiatry 142:98–100, 1985.
- Gardner DL, Cowdry RW. Positive effects of carbamazepine on behavioral dyscontrol in borderline personality disorder. *Am J Psychiatry* 143:519–522, 1986.
- Goveas JS, Csernansky JG, Coccaro EF. Platelet serotonin content correlates inversely with life history of aggression in personality-disordered subjects. Psychiatry Res 126:23–32, 2004.
- Hollander E, Tracy KA, Swann AC et al. Divalproex in the treatment of impulsive aggression: Efficacy in cluster B personality disorders. *Neuropsychopharmacology* 28:1186–1197, 2003.
- Ireland JL, Culpin V. The relationship between sleeping problems and aggression, anger, and impulsivity in a population of juvenile and young offenders. *J Adolesc Health* 38:649–655, 2006.
- Judge TA, Scott BA, Ilies R. Hostility, job attitudes, and workplace deviance: Test of a multilevel model. *J Appl Psychol* 91:126–138, 2006.
- Kessler RC, Chiu WT, Demler O et al. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 62:617–627, 2005.

- 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 63:669–678, 2006
- Laurent HK, Kim HK, Capaldi DM. Interaction and relationship development in stable young couples: Effects of positive engagement, psychological aggression, and withdrawal. J Adolesc 31:815–835, 2007.
- Lawrence E, Bradbury TN. Trajectories of change in physical aggression and marital satisfaction. J Fam Psychol 21:236–247, 2007.
- Linnoila M, Virkkunen M, Scheinin M et al. Low cerebrospinal fluid 5-hydroxyindoleacetic acid concentration differentiates impulsive from nonimpulsive violent behavior. *Life Sci* 33:2609–2614, 1983.
- Mattes JA. Comparative effectiveness of carbamazepine and propranolol for rage outbursts. *J Neuropsychiatry Clin Neurosci* 2:159–164, 1990.
- McCloskey MS, Berman ME, Broman-Folks J et al. Preliminary reliability and validity of the Intermittent Explosive Disorder Diagnostic Questionnaire (IED-DQ). *Assessment* (submitted).
- McCloskey MS, Berman ME, Noblett KL et al. Intermittent explosive disorder-integrated research diagnostic criteria: Convergent and discriminant validity. *J Psychiatr Res* 40:231–242, 2006.
- McCloskey MS, Kleabir K, Chen EY et al. Unhealthy aggression: The association between intermittent explosive disorder and negative health outcomes. *Health Psychol* (submitted).
- McCloskey MS, Lee R, Berman ME et al. The relationship between impulsive verbal aggression and intermittent explosive disorder. *Aggress Behav* 34:51–60, 2008a.
- McCloskey MS, Noblett KL, Deffenbacher JL et al. Cognitive-behavioral therapy for intermittent explosive disorder: A pilot randomized clinical trial. *J Consult Clin Psychol* 76:876–886, 2008b.
- McCloskey MS, Phan KL, Angstadt M et al. Amygdala hyperactivation to angry faces in intermittent explosive disorder. *Neuropsychopharmacology* (submitted).
- McElroy SL, Soutullo CA, Beckman DA et al. DSM-IV intermittent explosive disorder: A report of 27 cases. *J Clin Psychiatry* 59:203–210; quiz 211, 1998.
- Miller TQ, Markides KS, Chiriboga DA et al. A test of the psychosocial vulnerability and health behavior models of hostility: Results from an 11-year follow-up study of Mexican Americans. *Psychosom Med* 57:572–581, 1995.
- New AS, Hazlett EA, Buchsbaum MS et al. Blunted prefrontal cortical 18fluorodeoxyglucose positron emission tomography response to meta-chlorophenylpiperazine in impulsive aggression. *Arch Gen Psychiatry* 59:621–629, 2002.
- New AS, Trestman RF, Mitropoulou V et al. Low prolactin response to fenfluramine in impulsive aggression. *J Psychiatr Res* 38:223–230, 2004.
- Ortega AN, Canino G, Alegria M. Lifetime and 12-month intermittent explosive disorder in Latinos. *Am J Orthopsychiatry* 78:133–139, 2008.
- Ratey JJ, Sorgi P, O'Driscoll GA et al. Nadolol to treat aggression and psychiatric symptomatology in chronic psychiatric inpatients: A double-blind, placebo-controlled study. J Clin Psychiatry 53:41–46, 1992.
- Salzman C, Wolfson AN, Schatzberg A et al. Effect of fluoxetine on anger in symptomatic volunteers with borderline personality disorder. *J Clin Psychopharmacol* 15:23–29, 1995.
- Sheard MH, Marini JL, Bridges CI et al. The effect of lithium on impulsive aggressive behavior in man. Am J Psychiatry 133:1409–1413, 1976.
- Siever LJ, Buchsbaum MS, New AS et al. d, l-fenfluramine response in impulsive personality disorder assessed with [18F]fluorodeoxyglucose positron emission tomography. Neuropsychopharmacology 20:413–423, 1999.
- Soloff PH, George RS, Nathan PM et al. Paradoxical effects of amitriptyline on borderline patients. *Am J Psychiatry* 143:1603–1605, 1986.
- Swann AC. Treatment of aggression in patients with bipolar disorder. *J Clin Psychiatry* 60(suppl 15): 25–28, 1999.
- Tafrate RC. Evaluation of strategies for adult anger disorders, in *Anger Disorders: Definition, Diagnosis* & *Treatment*. Edited by Kassinove H. Washington, DC: Taylor & Francis, 1995, pp. 109–130.
- Vahtera J, Kivimäki M, Koskenvuo M et al. Hostility and registered sickness absences: A prospective study of municipal employees. *Psychol Med* 27:693–701, 1997.
- 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* 51:20–27, 1994.

- Volavka J, Citrome L. Aggression, alcohol and other substances of abuse, in *Neurobiology and Clinical Views on Aggression and Impulsivity*. Edited by Maes M, Coccaro E. London: Wiley, 1998, pp. 29–45.
 Wells S, Graham K, West P. Alcohol-related aggression in the general population. *J Stud Alcohol* 61:626–632, 2000.
- World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva: World Health Organization, 1992.
- Yudofsky S, Silver J, Schneider S. Pharmacologic treatment of aggression. *Psychiatr Ann* 17:397–406, 1987.