Intermittent Explosive Disorder-Revised: Development, Reliability, and Validity of Research Criteria

Emil F. Coccaro, Richard J. Kavoussi, Mitchell E. Berman, and Jennifer D. Lish

The study of human aggression has been hindered by the lack of reliable and valid diagnostic categories that specifically identify individuals with clinically significant displays of impulsive aggressive behavior. DSM intermittent explosive disorder (IED) ostensibly identifies one such group of individuals. In its current form, IED suffers from significant theoretical and psychometric shortcomings that limit its use in clinical or research settings. This study was designed to develop a revised criteria set for IED and present initial evidence supporting its reliability and validity in a well characterized group of personality disordered subjects. Accordingly, research criteria for IED-Revised (IED-R) were developed. Clinical, phenomenologic, and diagnostic data from 188 personality disordered individuals were reviewed. IED-R diagnoses were assigned using a best-estimate process. The reliability and construct validity of IED-R were examined. IED-R diagnoses had high interrater reliability (kappa = .92). Subjects meeting IED-R criteria had higher scores on dimensional measures of aggression and impulsivity, and had lower global functioning scores than non–IED-R subjects, even when related variables were controlled. IED-R criteria were more sensitive than DSM-IV IED criteria in identifying subjects with significant impulsive-aggressive behavior by a factor of four. We conclude that in personality disordered subjects, IED-R criteria can be reliably applied and appear to have sufficient validity to warrant further evaluation in field trials and in phenomenologic, epidemiologic, biologic, and treatment-outcome research.

DESPITE THE COMMON OCCURRENCE of inappropriate, impulsive-aggressive behaviors in our society, the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) continues to be deficient in identifying individuals with problematic behaviors of this type.[1] Although aggressive behaviors are sometimes observed in individuals diagnosed with established DSM major mental disorders (e.g., schizophrenia, bipolar disorder), clinical experience suggests that many nonpsychotic/nonbipolar (e.g., personality-disordered) individuals have clinically significant impulsive-aggressive behaviors that cannot be specifically identified by a DSM diagnostic category.[1]

The clinical relevance of impulsive-aggressive behavior is underscored by the many studies conducted in this area in the last two decades. First, impulsive-aggressive behavior is associated with compromised central serotonergic (5-HT) system functioning.[2] Second, data from family history,[3-5] and twin studies[6-8] provide evidence for a genetic component for aggressivity and impulsivity. Third, impulsive-aggressive behavior can be treated by both pharmacologic[9] and psychotherapeutic interventions.[10] To date, clinical trials have provided evidence that agents such as lithium,[11] carbamazepine,[12] and fluoxetine[13-15] can reduce impulsive-aggressive behavior. In addition, other agents, such as amitriptyline[16] and alprazolam[17] have been found to increase impulsive-aggressive behavior.

Currently, the only recognized set of DSM diagnostic criteria set to describe nonpsychotic/nonbipolar aggressive individuals is intermittent explosive disorder (IED). Serious theoretical and practical shortcomings limit the usefulness of both the DSM-III-R and DSM-IV IED criteria sets for categorizing individuals exhibiting clinically significant problems with aggressive behavior. For example, if DSM-III-R criteria for IED are applied, most individuals who have clear problems with impulsive-aggressive behavior will not be assigned this diagnosis.[18] This is due, in part, to the narrow definition of IED in DSM-III-R, which excludes individuals who are impulsive and aggressive between periods of more serious outbursts. This criterion was eliminated in DSM-IV, broadening the definition of IED.

Despite this modification, DSM-IV IED continues to be a problematic diagnostic entity. First, the diagnosis of IED is only allowable in individuals who commit severe acts of aggression (e.g., serious physical assault, destruction of objects). Many individuals with impulsive-aggressive behaviors

From the Clinical Neuroscience Research Unit, Department of Psychiatry, MCP-Hahnemann School of Medicine, Allegheny University of the Health Sciences, Philadelphia, PA; and The University of Southern Mississippi, Hattiesberg, MS.

Supported in part by NIMH Grants No. RO1MH46948, RO1MH47495 and KO2MH00951 to E.F.C.

Address reprint requests to Emil F. Coccaro, M.D., Clinical Neuroscience Research Unit, Department of Psychiatry, MCP-Hahnemann School of Medicine, 3200 Henry Ave, Philadelphia, PA 19129.

0010-440X/98/3906-0004$03.00/0

commit less severe acts of aggression, which, nonetheless, are associated with subjective distress, functional impairment, or legal problems. Second, a diagnosis of IED cannot be made in individuals also diagnosed with either antisocial (AsPD) or borderline (BPD) personality disorder. Although several individuals diagnosed with AsPD or BPD will behave aggressively from time to time, not all individuals carrying these diagnoses have a prominent history of impulsive-aggressive behavior. Failure to identify impulsive-aggressive behavior as the primary clinical concern will lessen the chance of treatment targeted specifically to these behaviors.

Given the problems with the current diagnostic criteria set for IED, we are proposing a revision of the DSM criteria for IED for research purposes so that individuals with frequent impulsive-aggressive behaviors, which are severe enough to lead to significant subjective distress or functional impairment, can be more accurately identified for study. After formulation of these criteria, we examined the interrater reliability and the behavioral correlates of this research diagnosis in a series of 188 personality-disordered patients.

METHODS

Subjects

This report provides data from 188 subjects meeting DSM-III-R[19] criteria for personality disorder (men, n = 140; women, n = 48) systematically evaluated in regard to aggressive, suicidal, self-injurious, and other behaviors as part of a larger program designed to study the biological and treatment correlates of impulsive-aggressive behavior in personality-disordered subjects. Subjects were recruited for this study by newspaper and public service announcements that sought subjects with anger and aggression problems and, for comparison, subjects without self-reported anger or aggression problems. Written informed consent, using an institutional review board–approved consent document, was obtained from all subjects after all procedures were fully explained.

Diagnostic Entry Criteria and Assessment

Only personality disorder subjects were eligible for study; subjects with a life history of mania/hypomania, schizophrenia, delusional disorder, current alcoholism, or drug use disorder were excluded from this study. Axis I and axis II personality disorder diagnoses were made according to DSM-III-R criteria (note: because data collection began in the DSM-III-R era, only DSM-III-R diagnoses are reported, except in the case of IED, in which both DSM-III-R and IV diagnoses are reported). Diagnosis of alcoholism was made by modified Research Diagnostic Criteria as in our previous reports.[20,21] Final diagnoses were assigned through a best-estimate process[22,23] with two psychiatrists and three psychologists based on information obtained through the following: (1) interviews by trained clinicians using the Schedule for Affective Disorders and Schizophrenia (SADS)[24] and the Structured Interview for the Diagnosis of DSM-III-R Personality Disorder (SIDP-R)[25]; (2) clinical interviews by a research psychiatrist; and (3) review of all other available clinical data. One best-estimator reviewed all available information and summarized this information in a written narrative report with suggested diagnoses. This written report was then reviewed and final consensus best-estimate diagnoses (all axis I and II diagnoses both current and past as an adult) were assigned by the best-estimate board.

Formulation of Revised Criteria for IED

Proposed revised diagnostic criteria for IED (IED-R) are listed in Table 1. These criteria describe an individual with a history of recurrent aggressive behavior expressed verbally, indirectly at objects, or physically directed at other individuals. This behavior occurs in discrete outbursts, and, if not physically assaultive, must be judged to be intense in nature. In other words, for example, brief verbal arguments in which the individual simply raises his or her voice would not be rated as meeting this criteria; evidence of shouting and loss of control during the outburst would be necessary for this behavior to be rated as counting towards the IED-R diagnosis. The aggressive behavior occurs in response to a perceived provocation, but is clearly out of proportion to that provocation. The aggressive behavior is not premeditated and is not exploited for personal gain; it is therefore "impulsive" in nature.[26] The aggressive behavior is not better explained by psychosis, mania, major depression, substance use disorders, or general medical conditions. The behavior occurs at least twice weekly (or eight times in a month), and it must specifically be associated with distress to the individual or with evidence of impairment in social and/or occupational function.

Diagnostic Assessment Study for IED-R

IED-R diagnoses were made based on review of clinical charts, SADS and SIDP-R interviews, and the Overt Aggression Scale-Modified for outpatients (OAS-M).[27] The OAS-M as-

Table 1. Diagnostic Criteria for IED-R

A. Recurrent incidents of verbal or physical aggression towards other people, animals, or property.
B. The degree of aggressive behavior is out of proportion to the provocation.
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, etc.).
D. Aggressive outbursts occur twice a week, on average, for at least a period of 1 month.
E. Aggressive behavior is not better accounted for by mania, major depression, or psychosis. It is not solely due to the direct physiological effect of a substance (e.g., drug of abuse) or of a general medical condition (e.g., closed head trauma, Alzheimer's).
F. The aggressive behavior causes either marked distress (in the individual) or impairment in occupational or interpersonal functioning.

sesses the frequency and intensity of recent overt aggressive acts. IED-R diagnoses were assigned using the diagnostic best-estimate procedure described previously.

Construct Validity Study

Construct validity was explored by comparing the data on a variety of parameters in which IED-R subjects were expected to differ from non–IED-R subjects. Differences between the groups (i.e., IED-R > non–IED-R) were expected on measures of aggression, impulsivity, life history of suicide attempt and self-injurious behavior, and global function (i.e., IED-R < non–IED-R). Aggression was assessed by interview (Life History of Aggression: LHA Aggression Score[28] and self-report questionnaire (Buss-Durkee Hostility Inventory: BDHI Aggression Factor.[29] Impulsivity was assessed by self-report questionnaires of Eysenck (Impulsiveness Scale of the 17:17-IMP),[30] and Barratt (Impulsiveness Scale-Version 11).[31] History of suicide attempt (SA) and self-injurious behavior (SIB) was assessed by interview during the clinical and structured diagnostic interview process described previously. Average global function of subjects over the past year was assessed by the Global Assessment of Function scale (GAF).[19] Assessment of state depression and state anxiety were assessed using the Hamilton Depression Rating Scale (HAMD)[32,33] and the Spielberger State Anxiety Inventory (SSAI),[34] respectively.

Statistical Analysis

Statistical analysis employed Kappa coefficient, chi-square, and/or Fisher's exact test where appropriate, Student's *t* test, Pearson correlation, and univariate (ANOVA)/multivariate (MANCOVA) analysis of variance. Analyses of covariance (ANCOVA/MANCOVA) analyses, in which the effect of significantly intercorrelating variables could be accounted for, were also performed. Covariates in these ANCOVA/MANCOVA analyses were as follows: (1) for aggression/impulsivity variables: age, race, socioeconomic status (SES) class, number of current axis I/II disorders, for any current mood disorder, any dramatic cluster personality disorder BPD, and HAMD and SSAI scores; (2) for history of suicide attempt: female gender; any current mood disorder, past history of alcoholism; any dramatic cluster PD, BPD, histrionic PD, and HAMD and SSAI scores; (3) for history of self-injurious behavior: histrionic PD; and (4) for GAF score: age, SES class, number of current axis I/II disorders, any current mood disorder, any dramatic cluster personality disorder, BPD, and HAMD and SSAI scores. Finally, hierarchical multiple regression and logistic regression analysis were performed where appropriate. All statistical tests were conducted two-tailed using an alpha value of .05.

RESULTS

Demographic Characteristics of the Sample

Table 2 lists the demographic and behavioral rating data for the subjects as a function of research criteria for IED-R. IED-R and non–IED-R subjects did not differ by gender or SES. However, IED-R subjects were, on average, 5 years older than non–IED-R subjects and were more likely to be Caucasian than African-American.

Table 2. Demographic and Behavioral Data on IED-R and Non–IED-R Subjects

Variable	IED-R (n = 76)	Non–IED-R (n = 112)	*P*
Age (yr)	37.0 ± 9.3	32.5 ± 9.3	.001
Gender (% male)	74.1%	75.0%	.890
Race			.004
% White (n = 137)	48.9%	51.1%	
% Black (n = 46)	19.6%	80.4%	
% Other (n = 5)	0.0%	100.0%	
Hollingshead SES Class			
% I/II/III/IV/V	18/26/15/26/15	18/29/17/25/11	.964
GAF score	53.8 ± 9.2	61.0 ± 8.9	.001
Impulsivity			
Eysenck I7	10.4 ± 3.9	7.2 ± 4.4	.001
Barratt (BIS-11)	56.9 ± 16.8	48.7 ± 18.7	.013
Other-directed aggression			
LHA aggression	16.3 ± 5.7	8.1 ± 5.7	.001
BDHI aggression	32.0 ± 7.2	20.8 ± 8.6	.001
History of self-directed aggression			
Suicide attempt	16 (21.1%)	8 (7.1%)	.005
Self-injurious behavior	7 (9.2%)	2 (1.8%)	.032
Total HAMD	6.5 ± 4.6	4.7 ± 5.6	.055
Extracted HAMD-6	3.8 ± 2.8	2.1 ± 2.7	.002
Speilberger State Anxiety	46.3 ± 13.8	38.4 ± 13.5	.001

Interrater Reliability for IED-R Criteria

Fifty of the 188 (27%) patients were randomly selected for an independent diagnostic assessment for IED-R by a second rater who was not part of the best-estimate panel and who was not aware of the assigned diagnoses. The pre–best-estimate (i.e., suggested) diagnosis from these 50 cases were then compared with the independent diagnosis of the second blind rater. The kappa coefficient for the diagnosis of IED-R for the two independent raters, reviewing the same material, was 0.92.

Construct Validity: Measures of Other-Directed Aggression and Impulsivity

IED-R subjects had significantly greater raw scores than non–IED-R subjects on LHA-Aggression, on BDHI-Aggression, and on 17- and BIS-11-Impulsivity. (Table 2) ANCOVA confirmed that IED-R subjects scored higher than non–IED-R subjects on each of the "aggression" measures (LHA Aggression: $F[1, 71] = 22.52$, $P < .001$; BDHI Aggression: $F[1,76] = 23.65$, $P < .001$) even after accounting for the effect of all relevant intercorrelating variables. The findings using the "impulsivity" measures were less striking with

Table 3. Axis I Disorder Diagnoses of IED-R and Non–IED-R Subjects

Axis I Disorders	IED-R (n = 76)	Non–IED-R (n = 112)	χ^2	*P*
No. of current disorders	0.8 + 0.9	0.5 ± 0.8	—	.034
No. of past disorders	1.2 ± 1.3	0.9 ± 1.2	—	.130
Current history of:				
Any mood disorder	30 (39.5%)	25 (22.3%)	6.44	.011
Major depression	3 (3.9%)	6 (5.4%)	FET*	.741
Dysthymia	11 (14.5%)	6 (5.4%)	4.58*	.032
Depressive disorder-NOS	16 (21.1%)	15 (13.4%)	1.93*	.165
Any anxiety disorder	15 (19.7%)	14 (12.5%)	1.82	.178
Life history of:				
Any mood disorder	55 (72.4%)	50 (44.6%)	14.11	.001
Major depression	26 (34.2%)	28 (25.0%)	1.88†	.171
Dysthymia	13 (17.1%)	8 (7.1%)	4.53†	.033
Depressive disorder-NOS	20 (26.3%)	23 (20.5%)	0.86†	.354
Any anxiety disorder	21 (27.6%)	18 (16.1%)	3.68	.055
Alcoholism	28 (36.8%)	25 (22.3%)	4.72	.030
Drug use disorders (abuse/dependence)	28 (36.8%)	21 (18.8%)	7.69	.006

Abbreviation: FET, Fisher's exact test.

*Post-hoc χ^2 after significant 4 × 2 χ^2 test (χ^2 = 9.48, *df* = 3, *P* = .024).

†Post-hoc χ^2 after significant 4 × 2 χ^2 test (χ^2 = 19.08, *df* = 3, *P* < .001).

only a trend towards statistical significance for BIS-11 "impulsivity" (F[1,56] = 3.70, *P* = .061) and no significant difference on the I7 "impulsivity" (F[1,62] = 2.05, *P* = .16) measures. A MANCOVA analysis in which all aggression and impulsivity measures were examined simultaneously in the same subjects yielded the same result. Subsequent logistic regression using the LHA and BDHI aggression scores alone led to a correct classification of 78.2% of cases into IED-R and non–IED-R categories.

Construct Validity: History of Self-Directed Aggression

IED-R subjects were more likely than non–IED-R subjects to have a life history of SA and SIB (Table 2). However, when the relevant intercorrelating variables were included in an ANCOVA model, the relationship between IED-R and SA was nonsignificant (F[1,107] = 2.18, *P* = .143). Similar ANCOVA analyses with SIB showed a marginally significant relationship with IED-R (F[1,187] = 3.94, *P* = .049). When LHA and BDHI "aggression" scores were added to the ANCOVA model, this relationship became statistically nonsignificant (F[1,155] = 2.20, *P* = .140). This suggests that the difference in SIB status among IED-R subjects was accounted for by differences in other-directed aggression.

Construct Validity: Global Function

In addition to having higher scores on various measures of aggression and impulsivity, IED-R subjects had significantly lower GAF scores than non–IED-R subjects (Table 2). A significant main effect for IED-R on GAF scores was found even after including relevant intercorrelating variables in the ANCOVA model (F[1,76] = 5.42, *P* = .023). When the LHA and BDHI "aggression" scores were added to the ANCOVA model, GAF no longer displayed a significant relationship with IED-R (F[1,69] = 1.22, *P* > .27). This suggests that differences in GAF scores as a function of IED-R status were accounted for by differences in other-directed aggression.

Discriminant Validity: Axis I Disorders

IED-R subjects had more current, and a trend towards more past, axis I disorders than non–IED-R subjects (Table 3). Among current axis I disorders, IED-R subjects were more likely than non–IED-R subjects to have a comorbid mood disorder of some type (39.5 *v* 22.3%); there was no difference between the groups in the frequency of other current axis I disorders (Table 3). This was accounted for by a greater frequency of dysthymia (14.5 *v* 5.4%) among IED-R compared with non–IED-R subjects. IED-R subjects were also more likely to have had a life history of a depressive disorder of any type (72.4 *v* 44.6%). This was again

accounted for by an excess of dysthymia in IED-R subjects. IED-R subjects were also more likely than non–IED-R subjects to have had a life (i.e., past) history of alcoholism or drug use disorder. Notably, MANCOVA analysis, including current/past history of any type of mood disorder and life history of alcoholism/drug use disorder, also showed elevated LHA and BDHI "aggression" scores in IED-R subjects (Wilks $\lambda = .68$, $F[2,55] = 12.72$, $P < .001$; LHA: $F[1,56] = 16,33$, $P < .001$; BDHI: $F[1,56] = 20.57$, $P < .001$).

Discriminant Validity: Axis II Personality Disorders

IED-R subjects had more axis II personality disorders than non–IED-R subjects (Table 4). Among the personality disorder diagnoses, IED-R subjects were more likely than non–IED-R subjects to meet DSM-III-R criteria for a dramatic cluster personality disorder. Among dramatic cluster diagnoses, IED-R subjects were far more likely than non–IED-R subjects to have BPD (there was a trend for an excess of histrionic personality disorder and AsPD). Despite this, BPD and AsPD, both of which exclude the diagnosis of DSM-III-R/IV IED, accounted for no more than 38% of all IED-R subjects. With the exception of the paranoid personality disorder (IED-R > non–IED-R), and the personality disorder–not otherwise specified diagnosis (non–IED-R > IED-R), the frequency of no other personality disorder diagnosis differed among IED-R and non–IED-R subjects.

Table 4. Axis II Personality Disorder Diagnoses of IED-R and Non–IED-R Subjects

Axis II Disorders	IED-R (n = 76)	Non–IED-R (n = 112)	χ^2	P
No. of axis II disorders*	2.1 ± 1.3	1.6 ± 1.1	—	.042*
Dramatic cluster	37 (48.7%)	31 (27.7%)	8.65	.004
Antisocial	11 (14.5%)	8 (7.1%)	2.68	.102
Borderline	25 (32.9%)	7 (6.3%)	22.76	.001
Histrionic	16 (21.0%)	13 (11.6%)	3.10	.079
Narcissistic	10 (13.2%)	10 (8.9%)	0.85	.356
Anxious cluster	27 (35.5%)	35 (31.3%)	0.37	.541
Avoidant	7 (9.2%)	7 (6.3%)	0.58	.448
Dependent	3 (3.9%)	3 (2.7%)	FET	.687
Obsessive-compulsive	13 (17.1%)	14 (12.5%)	0.78	.377
Passive-aggressive	11 (14.5%)	19 (17.0%)	0.21	.647
Eccentric cluster	20 (26.3%)	21 (18.8%)	1.52	.218
Paranoid	18 (23.7%)	14 (12.5%)	4.01	.045
Schizoid	3 (3.9%)	8 (7.1%)	FET	.530
Schizotypal	1 (1.3%)	5 (4.5%)	FET	.404
Not otherwise specified	19 (25.0%)	46 (41.1%)	5.17	.023

*Does not include subjects with personality disorder-NOS diagnoses.

Comparison Among DSM-III-R, DSM-IV and IED-R Criteria

Only three subjects in the total sample (2%) met DSM-III-R criteria for IED. Using DSM-IV criteria, however, a total of 19 subjects (10%) were identified (IED-R group I), representing a significant difference over DSM-III-R criteria ($z = 9.11$, $P < .001$). This was due to the removal of the criteria item excluding subjects with interepisodic aggressiveness and/or impulsiveness. Dropping the criteria item excluding subjects with BPD or AsPD identified an additional 27 subjects (IED-R group II), which brought the total to 46 subjects (25%); this represents a significant difference over DSM-IV criteria ($z = 6.41$, $P < .001$). Expanding the inclusion criteria item to allow significant verbal aggression and less severe physical aggression (i.e., not associated with serious injury of destruction of property) identified a final group of 30 subjects (IED-R group III) for a total of 76 subjects (40%)—a significant difference over the proportion of subjects identified by including groups I and II ($z = 5.03$, $P < .001$). Notably, MANCOVA analysis showed that LHA and BDHI "aggression" scores did not differ among subjects in IED-R groups I/II/III (Wilks $\lambda = .91$, $F[4,46] = 0.55$, $P = .703$).

DISCUSSION

These data provide initial evidence for the interrater reliability and construct validity for a research diagnosis of IED-R in a cohort of personality-disordered subjects. The high degree of interrater reliability is most likely due to the fact that the information required to make the diagnosis depends largely on the report, and/or observation, of behaviors and their consequences rather than report, or inference, of inner states related to anger or an attempt to resist "aggressive impulses."

Construct validity is suggested by several observations. Most importantly, subjects meeting research criteria for IED-R had higher scores on interview and self-reported measures of aggression and impulsivity. The difference between IED-R/non–IED-R groups is specific to outwardly directed aggressive behavior; neither history of SA nor SIB was more frequent in IED-R subjects after other relevant factors (including outwardly directed ag-

gression) were accounted for. This is in apparent contrast to primarily suicidal subjects in whom impulsivity, but not necessarily anger, has been reported as significantly elevated in comparison with control subjects.[35] Our data also suggest that aggression, rather than impulsivity alone (i.e., when both are in the same model), best accounts for variability in IED-R subjects. Rather than uniquely characterizing IED-R subjects, impulsiveness seems to describe the type of (or covary with) aggressive behavior displayed by these subjects. Confirmation that the aggressive behavior is associated with a clinically important reduction in function was provided by analyses that demonstrated that global function was lower among IED-R, compared with non–IED-R, subjects, and that adding aggression measures to the model eliminated this difference between the groups. Finally, no specific current axis I disorder was found to better account for IED-R. Although a current mood disorder (specifically dysthymia) was found in excess in IED-R subjects, this diagnosis was absent in most subjects. Further, even after accounting for a current or past history of mood disorder and the severity of state depression, aggression scores remained elevated in IED-R subjects. The same was true for both past history of alcoholism and other drug use disorders. Aggression scores remained elevated in IED-R subjects even when a life (i.e., past) history of these disorders was accounted for.

Broadening the Diagnostic Criteria for IED

As currently described in DSM-IV, IED cannot identify most subjects with clinically significant impulsive-aggressive behavior. In this study, only 25% of such-subjects (i.e., 19 of 76) would have met DSM-IV criteria for IED. Allowing for the diagnosis of BPD and AsPD, and allowing for less severe (though still clinically meaningful) aggressive behavior, identified the remaining subjects with a fourfold increase over current DSM-IV criteria. Each step in this process was associated with a statistically significant increase in the proportion of subjects identified as having clinically significant impulsive-aggressive behaviors.

Inclusion of Subjects With BPD and AsPD in IED-R

Both DSM-III-R and DSM-IV IED criteria and text indicate that the IED diagnosis should not be given in subjects who already meet criteria for BPD or AsPD. This rule places BPD/AsPD hierarchically above IED. Although such rules are integral to the organization of the DSM,[36] IED is one of the few instances where a personality disorder diagnosis excludes, or essentially excludes, an axis I diagnosis. Otherwise, personality disorder diagnoses are either made along with axis I diagnoses, or axis I diagnoses exclude personality disorder diagnoses (e.g., schizophrenia excludes paranoid, schizoid, and schizotypal personality disorders). The apparent reason for this variance in DSM hierarchy rules is that aggressive behavior is presumed to be common among these BPD/AsPD subjects, and, accordingly, BPD/AsPD diagnoses already identify these subjects. Two arguments can be made against this premise and the hierarchy implicit in this case. First, the overlap between IED and BPD/AsPD, in BPD/AsPD subjects specifically, is not great enough that the former diagnosis cannot be made without the latter. In our sample, 22% of BPD, and 42% of AsPD, subjects did not meet criteria for IED-R. Unlike the extensive overlap between generalized social phobia (GSP) and avoidant personality disorder (APD), the overlap between IED-R and BPD/AsPD, although substantial, is not complete. Even in the case of GSP/APD, where diagnostic overlap is essentially complete,[37] the axis II disorder (APD) does not preclude the axis I disorder (GSP). Second, existing biological and treatment response data do not strongly support BPD or AsPD as a more relevant entity under which impulsive aggressive behavior should be placed. If anything, these data support the reverse arrangement. For example, where BPD/AsPD subjects are reported to display evidence of reduced 5-HT function, this feature is due to the presence of impulsive-aggressive behavior and not to the presence of other BPD/AsPD characteristics.[20,38-40] Moreover, family history data suggest that the familial transmission of BPD is due to the transmission of two separate traits characterized by impulsive aggression and affective dysregulation.[41] Treatment response data are similar in this regard. Most psychopharmacologic agents have little, or only a modest, effect on general BPD/AsPD symptomatology.[9] Where effective, psychopharmacologic agents more specifically reduce symptomatology within dimensions of behavior rather than reduce all symptoms for the parent personality disorder.[42-45] In the case of aggression, for example, lithium carbonate has been shown to reduce impul-

sive aggressive, but not other antisocial, behaviors in prison inmates.[11] In a more recent study, diphenylhydantoin has been shown to reduce impulsive, but not premeditated/antisocial, aggression in prison inmates.[46] In addition, psychosocial interventions, targeted to treat BPD, are reported to reduce anger and parasuicidal behavior but little else specifically related to the BPD diagnosis.[10] Accordingly, biological and treatment response data suggest that impulsive-aggressive behavior, although present in BPD/AsPD subjects, has specific clinical relevance apart from the remaining diagnostic features of BPD/AsPD. Assigning an IED-R diagnosis, therefore, highlights the presence of clinically significant impulsive-aggressive behavior and allows for more specific treatment planning.

Broadening the Spectrum of Aggression in IED-R

IED, as defined by DSM-III-R and IV, only includes aggressive behavior involving serious aggression against persons (assault) and property (destruction). This narrow definition of aggression does not include recurrent verbal aggression or indirect aggression not associated with serious destructive behavior. We have included these types of aggressive behaviors in IED-R where they are intense, and where they reach a frequency and severity level associated with distress to the individual or impairment in interpersonal and/or occupational function. In other words, the IED-R diagnosis can only be made when these behaviors reach clinical significance. In this sample, 39% of IED-R subjects were identified (IED-R group III) by broadening this aspect of the diagnostic criteria. Supporting this approach, MANCOVA analysis showed that these subjects were, by BDHI and LHA "aggression" scores, generally as aggressive (if not physically assaultive/destructive) as DSM-IV IED (IED-R group I) subjects and as IED-R subjects with BPD/AsPD (IED-R group II). The clinical relevance of these nonphysically assaultive manifestations of aggressive behavior is highlighted by observations that these behaviors can be reduced by pharmacotherapy with serotonin uptake inhibitors.[13-15] Inclusion of these individuals into IED-R thus allows for the identification of subjects with clinically significant impulsive-aggressive behavior that may be responsive to treatment intervention. Without formal identification of this kind, treatment of impulsive-aggressive behaviors in these individuals will be inconsistent.

Caveats

The primary caveat for this study is that all subjects in this sample were personality disordered. This was because the primary study into which subjects were recruited required subjects to meet criteria for personality disorder. Accordingly, these data may not necessarily be generalized to potential IED-R subjects without personality disorder. However, since no study of IED has systematically evaluated for the presence of personality disorder,[47] the relative prevalence of personality disorder among IED subjects is unknown. Future studies which include IED-R subjects, regardless of the presence of a personality disorder, will be needed to determine if the data presented generalize to a non–personality-disordered sample.

In conclusion, the establishment of research criteria that improve the identification of individuals with persistent and specific difficulties with impulsive-aggressive behaviors should allow for further research in which these individuals can be more fully characterized in terms of phenomenology, epidemiology, familial/genetic transmission, biologic/psychologic features, and response to pharmacologic/psychologic treatment. Regarding the latter two areas of study, it should be noted that we have found that IED-R subjects demonstrate a blunted prolactin response to d-fenfluramine challenge (i.e., reflecting reduced central 5-HT activity; Coccaro et al, unpublished data in preparation) and manifest a specific antiaggressive response to fluoxetine under double-blind, placebo-controlled conditions.[15]

ACKNOWLEDGMENT

The authors acknowledge Lauren Weinberg, M.S.Ed., Lynn Gladis, Ph.D., and David Sawrer, Ph.D. for their contributions to the best-estimate procedures involved in the final assignment of subject diagnosis.

REFERENCES

1. Maiuro RD. Intermittent explosive disorder. In: Dunner DL (ed): Current Psychiatric Therapy. Philadelphia, PA: Saunders, 1996.

2. Coccaro EF, Kavoussi RJ. Neurotransmitter correlates of impulsive aggression. In: Stoff DM, Cairns RB (eds): The Neurobiology of Clinical Aggression. Mahwah, NJ: Erlbaum, 1996:67-85.

3. Mattes JA, Fink M. A family study of patients with temper outbursts. J Psychiatr Res 1987;21:249-255.

4. Mattes JA, Fink M. A controlled family study of adopted patients with temper outbursts. J Nerv Ment Dis 1990;178:138-139.

5. Coccaro EF, Silverman J, Klar HM, Horvath TB, Siever LJ. Familial correlates of reduced central serotonergic system function in patients with personality disorder. Arch Gen Psychiatry 1994;51:318-324.

6. Plomin R, Nitz K, Rowe DC. Behavioral genetics and aggressive behavior in childhood. In: Lewis M, Miller S (eds): Handbook of Developmental Psychopathology. New York, NY: Plenum, 1990:119-133.

7. Coccaro EF, Bergeman CS, McClearn G. Heritability of irritable impulsiveness: A study of twins reared together and apart. Psychiatry Res 1993;48:229-242.

8. Coccaro EF, Bergeman CS, Kavoussi RJ, Seroczynski A. Heritability of aggression and irritability: A twin study of the Buss-Durkee aggression scales in adult male subjects. Biol Psychiatry 1997;41:273-284.

9. Coccaro EF, Siever LJ. The neuropsychopharmacology of personality disorder. In: Bloom F, Kupfer D (eds): Psychopharmacology: The Fourth Generation of Progress. New York, NY: Raven, 1995.

10. Linehan MM, Tutek DA, Heard HL, Armstrong HE. Interpersonal outcome of cognitive behavioral treatment for chronically suicidal borderline patients. Am J Psychiatry 1994; 151:1771-1776.

11. Sheard M, Marini J, Bridges C, Wapner A. The effect of lithium on impulsive aggressive behavior in man. Am J Psychiatry 1976;133:1409-1413.

12. Gardner DI, Cowdry RW. Positive effect of carbamazepine on behavioral dyscontrol in borderline personality disorder. Am J Psychiatry 1986;143:519-522.

13. Fava M, Rosenbaum JF, Pava JA, McCarthy MK, Steingard RJ, Bouffides E. Anger attacks in unipolar depression, part 1: Clinical correlates and response to fluoxetine treatment. Am J Psychiatry 1993;150:1158-1163.

14. Salzman C, Wolfson AN, Schatzberg A, Looper J, Henke R, Albanese, et al. Effect of fluoxetine on anger in symptomatic vounteers with borderline personality disorder. J Clin Psychopharmacol 1995;15:23-29.

15. Coccaro EF, Kavoussi RJ. Fluoxetine and impulsive aggressive behavior in personality disordered subjects. Arch Gen Psychiatry 1997;54:1081-1088.

16. Soloff PH, George A, Nathan RS, Schulz PM, Perel, JM. Paradoxical effects of amitriptyline in borderline patients. Am J Psychiatry 1986;143:1603-1605.

17. Gardner DI, Cowdry RW. Alprazolam-induced dyscontrol in borderline personality disorder. Am J Psychiatry 1985;142: 98-100.

18. Felthous AR, Bryant G, Wingerter CB, Barratt ES. The diagnosis of intermittent explosive disorder in violent men. Bull Amer Acad Psychiatry Law 1991;19:71-79.

19. Spitzer RL (ed). The Diagnostic and Statistical Manual-Third Edition. Revised (DSM-III-R). Washington, DC: American Psychiatric Press, 1987.

20. Coccaro EF, Siever LJ, Klar H, Maurer G, Cochrane K, Cooper TB, et al. Serotonergic studies in affective and personality disorder patients: Correlates with suicidal and impulsive-aggressive behavior. Arch Gen Psychiatry 1989;46:587-599.

21. Coccaro EF, Kavoussi RJ, Sheline YI, Lish JD, Csernansky JG. Impulsive aggression in personality disorder: Correlates with ^{3}H-Paroxetine binding in the platelet. Arch Gen Psychiatry 1996;53:531-536.

22. Leckman JF, Sholomskas D, Thompson WD, Belanger A, Weissman MM. Best estimate of lifetime psychiatric diagnosis: a methodologic study. Arch Gen Psychiatry 1982;39:879-883.

23. Klein DN, Ouimette PC, Kelly HS, Ferro T, Riso LP. Test-retest reliability of a team consensus best-estimate diagnoses of axis I and II disorders in a family study. Am J Psychiatry 1994;151:1043-1047.

24. Spitzer RL, Endicott J. Schedule for Affective Disorders and Schizophrenia. New York, NY: NY State Psychiatric Institute, 1978.

25. Pfohl B, Zimmerman M. Structured Interview for DSM-III-R Personality Disorders. Iowa City, IA: University of Iowa College of Medicine, 1989.

26. Linnoila M, Virkkunen M, Scheinin M, Nuutila A, Rimon R, Goodwin FK. Low cerebrospinal fluid 5-HIAA concentration differentiates impulsive from nonimpulsive violent behavior. Life Sci 1983;33:2609-2614.

27. Coccaro EF, Harvey PD, Kupsaw-Lawrence E, Herbert JL, Bernstein DP. Development of neuropharmacologically based behavioral assessments of impulsive aggressive behavior. J Neuropsychiatry Clin Neurosci 1991;3:S44-S51.

28. Coccaro EF, Berman ME, Kavoussi RJ. Assessment of life history of aggression: Development and psychometric characteristics. Psychiatry Res 1997;73:147-157.

29. Buss AH, Durkee A. An inventory for assessing different kinds of hostility. J Consult Psychol 1957;21:343-348.

30. Eysenck SBG, Eysenck HJ. The place of impulsiveness in a dimensional system of personality discription. Br J Soc Clin Psychol 1977;16:57-68.

31. Patton JH, Stanford MS, Barratt ES. Factor structure of the Barratt Impulsiveness Scale. J Clin Psychol 1995;51:768-774.

32. Guy W. ECDEU Manual for Psychopharmacology. Washington, DC: Superintendent of Documents, US Government Printing Office; US Department of Health, Education, and Welfare publication ADM 76-338;1976.

33. O'Sullivan RL, Fava M, Agustin C, Baer L, Rosenbaum JF. Sensitivity of the six-item Hamilton Depression Rating Scale. Acta Psychiatr Scand 1997;95:379-384.

34. Spielberger CD. Manual for the State-Trait Anxiety Inventory: STAI (Form Y). Palo Alto, CA: Consulting Psychologists Press, 1983.

35. Horesh N, Rolnick T, Iancu I, Dannon P, Lepkifer E, Apter A, et al. Anger, impulsivity and suicide risk. Psychother Psychosom 1997;66:92-96.

36. First MB, Spitzer RL, Williams JBW. Exclusionary principles and the comorbidity of psychiatric diagnoses: A historical review and implications for the future. In: Maser JD, Cloninger CR (eds): Comorbidity of Mood and Anxiety Disorders, Washington, DC: American Psychiatric Press, 1990:83-109.

37. Widiger TA. Generalized social phobia versus avoidant personality disorder: A commentary on three studies. J Abnorm Psychol 1992;101:340-343.

38. Brown GL, Ebert MH, Goyer PF, Jimerson DC, Klein WJ, Bunney WE, et al. Aggression, suicide, and serotonin: Relationships to CSF amine metabolites. Am J Psychiatry 1982;139:741-746.

39. Moss HB, Yao JK, Panzak GL. Serotonergic responsivity and behavioral dimensions in antisocial personality disorder with substance abuse. Biol Psychiatry 1990;28:325-338.

40. O'Keane V, Moloney E, O'Neill H, O'Connor A, Smith C, Dinan TG. Blunted prolactin responses to d-fenfluramine in sociopathy: Evidence for subsensitivity of central serotonergic function. Br J Psychiatry 1992;160:643-646.

41. Silverman JM, Pinkham L, Horvath TB, Coccaro EF, Klar HM, Schear S, et al. Affective and impulsive personality disorder traits in the relatives of borderline personality disorder. Am J Psychiatry 1991;148:1378-1385.

42. Goldberg SC, Schulz SC, Schulz PM, Resnick RJ, Hamer RM, Friedel RO. Borderline and schizotypal personality disorders treated with low-dose thiothixine versus placebo. Arch Gen Psychiatry 1986;43:680-686.

43. Cowdry RW, Gardner DL. Pharmacotherapy of borderline personality disorder: Alprazolam, carbamazepine, trifluroperazine, and tranycypromine. Arch Gen Psychiatry 1988;45: 111-119.

44. Soloff PH, George A, Nathan RS, Schulz PM, Cornelius JR, Herring J, et al. Amitriptyline versus haloperidol in borderlines: Final outcomes and predictors of response. J Clin Psychopharmacol 1989;9:238-246.

45. Soloff PH, Cornelius JR, George A, Nathan RS, Schulz PM, Perel JM, et al. Efficacy of phenelzine and haloperidol in borderline personality disorder. Arch Gen Psychiatry 1993;50: 377-385.

46. Barratt ES, Stanford MS, Felthous AR, Kent TA. The effects of phenytoin on impulsive and premeditated aggression: A controlled study. J Clin Psychopharmacol 1997;17:341-349.

47. Bradford J, Geller J, Lesieur HR, Rosenthal R, Wise M. Impulse control disorders. In: Widiger TA, Frances AJ, Pincus HA, First MB, Ross R, Davis W (eds): *DSM-IV Sourcebook, Vol. II.* Washington, DC: American Psychiatric Press, 1994:1007-1031.