



Antisocial personality and bipolar disorder: interactions in impulsivity and course of illness

Alan C Swann*

Practice points

- Bipolar disorder and antisocial personality disorder (ASPD) appear to overlap, with greater severity in the combined disorders.
- In ASPD, it is important to be aware of the potential for suicidal behavior and mood instability.
- In bipolar disorder, it is important to be aware of the potential for criminal and impulsive–aggressive behavior, and that these characteristics are associated with increased suicidal behavior.
- In bipolar disorder, presence of ASPD characteristics is associated with early-onset, severe recurrence and predominately manic course.
- Mood-stabilizing medicines and behavioral treatments aimed at impulsivity, aggression and substance use can be helpful across both disorders.

SUMMARY Antisocial personality disorder (ASPD) and bipolar disorder are both characterized by impulsive behavior, increased incarceration or arrest, addictive disorders and suicidal behavior. These characteristics appear more severe in the combined disorders. Individuals with ASPD who also have bipolar disorder have higher rates of addictive disorders and suicidal behavior and are more impulsive, as measured by questionnaires or behavioral laboratory tests. Those with bipolar disorder who have ASPD have higher rates of addictive, criminal and suicidal behavior, earlier onset of bipolar disorder with a more recurrent and predominately manic course and increased laboratory-measured, but not questionnaire-rated, impulsivity. These characteristics may result in part from differential impulsivity mechanisms in the two disorders, with bipolar disorder driven more by excessive catecholamine sensitivity and ASPD by deficient serotonergic function.

Dimensions that cut across psychiatric illnesses

Our nosological system is based on descriptively defined clinical syndromes. Brain systems governing fundamental aspects of behavior underlie these entities. One interesting challenge in

psychiatry is the manner in which dysregulation of systems governing basic aspects of behavior may cut across recurrent psychiatric disorders and personality disorders. These relationships contribute to diagnostic and treatment dilemmas. For example, bipolar disorder and cluster B

*Department of Psychiatry, Houston Health Science Center, 1300 Moursund Street, Room 270, Houston, TX 77030, USA; Tel.: +1 713 486 2555; Fax: +1 713 486 2553; alan.c.swann@uth.tmc.edu

personality disorders could be part of a continuum [1], as originally suggested by Kraepelin [2]. Alternatively, they could represent disorders that share important clinical features but have distinct mechanisms that combine dimensionally in severe cases [3–7].

Cluster B personality disorders and bipolar disorder share impulsivity as a core feature [3,8]. Substance abuse, suicidality and criminal behavior, potentially related to impulsivity, cut across antisocial personality disorder (ASPD) and bipolar disorder [8]. Yet there is only limited information comparing impulsivity and its mechanisms in bipolar disorder with personality disorders.

■ Characteristics & mechanisms of impulsivity

Impulsivity may represent an imbalance between behavioral activation and inhibition [9]. It can be measured by questionnaires, such as the Barratt Impulsiveness Scale (BIS-11). The BIS-11, developed over a 50-year period, measures three aspects of trait impulsivity: affective and cognitive instability ('attentional'); acting on the spur of the moment ('motor'); and lack of future sense ('nonplanning'). Questionnaires rely on recall and interpretation of behavior and attitudes, and are therefore subject to bias.

Human behavioral-laboratory measures have been developed that measure aspects of cognitive performance related to animal models of impulsivity, without the biases of questionnaires [10,11], including:

- Rapid-response impulsivity represents an inability to adequately evaluate a stimulus before responding to it, or to conform responses to their context. Measurements include: continuous performance tests, where a subject must typically respond if a stimulus matches a relatively complex test stimulus given every 500 ms, and a response to a stimulus almost matching the test stimulus is considered impulsive; or stop-signal tasks, where a subject must inhibit a prepotent response [10,11]. Noradrenergic stimulation increases rapid-response impulsivity in healthy controls [12] and in rats [13]; this is a proposed mechanism of poor impulse control in post-traumatic stress disorder [14]. Serotonin counteracts catecholamine effects on rapid-response impulsivity; for example, stimulation of postsynaptic 5-HT_{1A} receptors decreases correct detections and slows response times in rats [15].

- Reward-delay impulsivity, or inability to delay response for a larger reward, is based on the idea that impulsivity is characterized by an acceleration in the normal loss of value of a reward over time (called 'delay discounting'), and is measured by tasks requiring a choice between smaller-sooner and larger-later rewards [10,11].

- Rapid-response and reward-delay impulsivity are increased in bipolar disorder, especially with recurrent or complicated courses of illness [5]. They are also components of low self-control, which is relevant to criminal behavior [16,17].

Methods

In order to explore this topic, we conducted a related series of literature searches in Medline, using, as key words or as items in indexed fields, bipolar disorder and ASPD or crime and: impulsive behavior or impulse control disorders or response inhibition; family or genetics or gene expression; suicide or attempted suicide; and diagnosis. In addition, we used other papers cited in articles from these searches, or cited in articles used in our own work.

Why bipolar disorder & ASPD?

■ Rationale: possible relationships between bipolar disorder & ASPD

Table 1 compares characteristics of ASPD and bipolar disorder. The disorders have similar prevalence and suicide mortality, and both have widespread comorbid addictive disorders. Ages of onset are typically lower in ASPD, but they overlap with bipolar disorder. After discussing familial evidence regarding overlap between ASPD and bipolar disorder, we will address mechanisms of impulsivity in bipolar disorder and in ASPD, and will then compare them and discuss properties of apparently combined ASPD and bipolar disorder.

■ Evidence for familial or genetic relationships between ASPD & bipolar disorder

Results of some family aggregation studies have suggested that common mechanisms may cut across bipolar disorder, substance-use disorders and cluster B personality disorders. The Family Collection of the Collaborative Study on the Genetics of Alcoholism, using age-corrected lifetime morbid risk estimates in adult first-degree relatives of probands with alcohol-use

disorders (n = 8296) and controls (n = 1654) found an aggregation of ASPD, drug dependence, anxiety disorders and mood disorders [18]. Similarly, a family interview study found extensive coaggregation among borderline personality disorder, other cluster B personality disorders, affective disorders and substance-use disorders, suggesting common familial factors, particularly in the areas of affective disturbance and impulsivity [19].

A study of 140 ADHD and 120 normal controls at baseline and 4 years later found that ADHD children with both conduct disorder (CD) and bipolar disorder had higher familial and personal risk for mood disorders than those with CD only, with poorer functioning and an increased risk for psychiatric hospitalization. These results suggested the possibility of a dysphoric subtype of CD that might represent a CD–bipolar disorder combination [20]. The study found a three-way association of familial predisposition to ADHD, ASPD and bipolar disorder, suggesting to the authors that antisocial- and bipolar-ADHD subtypes were different manifestations of the same specific familial form of ADHD [21].

Studies focusing primarily on bipolar and antisocial disorders (ASPD and CD) have suggested a greater specificity. Comparing relatives of children with CD and/or bipolar disorder to controls, Wozniack and coworkers found high rates of CD/ASPD and bipolar disorder in relatives of children with combined CD and bipolar disorder [22]. The combination of CD/ASPD and bipolar disorder was found exclusively among relatives of children with combined disorders and not in those with CD or bipolar disorder alone, suggesting that CD/ASPD and bipolar disorder represent separate disorders, and that “the combination of CD and bipolar disorder may be a distinct nosological entity.” Similarly, a blinded, controlled family study using structured diagnostic interviews of 157 children with bipolar I disorder (487 first-degree relatives), 162 having ADHD without bipolar I disorder (511 first-degree relatives) and 136 healthy controls (411 first-degree relatives) found that relatives of children with bipolar I disorder had high rates of ASPD compared with relatives of controls, but the effect lost significance after correcting for the presence of CD/ASPD in the proband [23].

Therefore, family studies suggest that bipolar and ASPD may be disorders sharing common characteristics (e.g., impulsivity), that bipolar

disorder and ASPD may be disorders with different mechanisms for similar symptoms and that the apparent combination of bipolar disorder and ASPD may be an independent disorder. Focusing on impulsivity, we will investigate evidence for and implications of these possibilities.

Impulsivity in bipolar disorder

■ Trait impulsivity

Questionnaire-rated impulsivity, measured by BIS-11, is elevated in bipolar disorder [24–27]. This is especially true with severe course of illness, reflected by many episodes, comorbid substance-use disorders and suicide attempts [28].

■ Laboratory performance impulsivity

Rapid-response impulsivity is increased in bipolar disorder in the presence of mania [29–31], co-occurring addictive disorder [32] or recurrent course of illness [5]. Reaction times are slow in euthymic bipolar disorder [5,33,34], and response bias is conservative [5]. These characteristics appear counterintuitive for bipolar disorder and may reflect a compensatory mechanism reducing commission errors at the expense of reductions in response speed and correct detections [15]. Reaction times are faster and impulsive error rates greater with recurrent illness [5] or history of a medically severe suicide attempt [35], suggesting that this compensatory mechanism may be absent or may fail in more severe bipolar disorder [5].

Gender has no effect on impulsivity [5,28] or conviction history in bipolar disorder [36]. Approximately 90% of individuals with ASPD are men, but half of those with comorbid ASPD and bipolar disorder were women [37]. These findings resemble relationships between gender and alcohol abuse [38] or suicide [39,40]: the normal preponderance of men is reduced in bipolar disorder, with increased relative risk for women, compared with the general population.

Table 1. Bipolar disorder and antisocial personality disorder: clinical features.

	ASPD	Bipolar disorder
Prevalence	3.3% [129]	1–6% depending on definition of hypomania [130]
Gender	90% men	50% men
Typical onset	Childhood	Adolescent–young adult
Range of onsets	Childhood–adulthood	Lifespan, including childhood
Substance-use disorder	80–90%	60%
Suicide mortality	10%	10%

ASPD: Antisocial personality disorder.

■ Mechanisms of impulsivity in bipolar disorder

Bipolar disorder confers increased sensitivity to behaviorally activating effects of catecholamines [41,42]. Increased noradrenergic function in mania correlates with manic symptoms [43], as does rapid-response impulsivity [27]. The prefrontal cortical and anterior cingulate gyrus, involved in behavioral monitoring and error checking, are inhibited by excessive noradrenergic stimulation [44–47]. Serotonergic function in uncomplicated bipolar disorder appears relatively intact [43,48], providing a potential mechanism to compensate for increased norepinephrine [15].

■ Impulsivity & course of illness

Recurrence

Most episodes of bipolar disorder are depressive [49], but there are predominately depression- and mania-prone forms [50]. Increased frequency or number of episodes of either depression or mania in bipolar disorder are associated with increased questionnaire-measured [28] or rapid-response [5] impulsivity.

Comorbid conditions

History of an addictive disorder is associated with greater questionnaire-measured and rapid-response impulsivity in bipolar disorder [32]. Anxiety is also correlated with impulsivity in bipolar disorder [51,52].

Suicidal behavior

Suicidal behavior in bipolar disorder is increased with substance-use disorders [53–55], severely recurrent illness [5,56], comorbid ASPD or cluster B personality disorders [37,51] and rapid-response impulsivity [35]. Multivariate analysis showed that rapid-response impulsivity was associated with medically severe suicide attempts, even after effects of addictive disorders were taken into account [35].

■ Summary: impulsivity in bipolar disorder

- Questionnaire-measured impulsivity is substantially increased in bipolar disorder regardless of treatment or clinical state. Questionnaire-measured impulsivity is increased further in severely recurrent or complicated bipolar disorder.
- Rapid-response impulsivity is increased in bipolar either during mania or with severely complicated or recurrent illness. Euthymic patients

with milder illness may compensate for potentially increased rapid-response impulsivity by responding more slowly and conservatively. Note that this compensation is not conscious but occurs on the scale of tenths of a second.

- Increased impulsivity in bipolar disorder is associated with risk for addictive and suicidal behavior.

Impulsivity & ASPD

■ Trait impulsivity

Impulse behavior is prominent in cluster B personality disorders, including ASPD [57,58]. ASPD is characterized by poor impulse control, suicide and destructive behavior [59], beginning in childhood and persisting into adulthood [57].

Impulsivity appears to underlie all cluster B personality disorders, which are differentiated by characteristics related to aggression, culture and gender [60–62]. In a large nonclinical sample of adolescents, self-reported impulsivity correlated with antisocial behavior and predicted future increases in antisocial behavior [63]. Impulsivity strongly predicted psychopathy and conduct problems in adolescents in a maximum-security facility [64].

Questionnaire-rated impulsivity (BIS-11) [65] is increased in adults with histories of CD [66], adults with ASPD or with adult antisocial behavior [67,68] and in adolescents with disruptive behavior disorders [10] and their parents [11]. BIS-11 motor impulsiveness, related to acting without thinking, was increased in subjects with ASPD identified in a nonclinical sample [62], and correlated with symptoms of ASPD and borderline personality disorder [62,69]. Similarly, subjects with ASPD performed normally on the Iowa Gambling Task (a measure of decision-making), but had impaired performance in a Stroop test designed to measure impulsivity [70].

■ Laboratory-measured impulsivity

Response inhibition is impaired in ASPD [71]. On a measure of rapid-response impulsivity, subjects with ASPD had more impulsive response bias than controls; impulsive error rates and response bias correlated with severity of ASPD, although self-reported impulsivity did not [68]. Impulsive behavior and rapid-response impulsivity appear related to deficits in serotonergic function in ASPD [72–75].

In addictive disorders, reward-delay impulsivity was increased if ASPD was also present;

there were no subjects in this study with ASPD alone [76]. Similarly, reward-delay impulsivity was increased in cocaine dependence, but only with a history of aggressive behavior [77].

■ Mechanisms of impulsivity in ASPD

In ASPD, functional serotonergic capacity is reduced [72,78,79]. Reward-delay impulsivity is increased by serotonin depletion or blockade [80,81], especially in CD or ASPD [79,80]. There is disagreement about the role of potentially hypersensitive dopaminergic reward systems [82,83]. The consensus is that behavioral problems in ASPD, including those related to impulsivity [74] and to reward processing [75], stem from serotonergic deficits.

Unlike bipolar disorder, ASPD is characterized by hypoarousal [84]. Noradrenergic function and reactivity is normal or reduced in ASPD [85–87]; unlike bipolar disorder, noradrenergic and autonomic responses to stressors are reduced in subjects with ASPD [87–89] and their offspring [90].

Impulsivity, therefore, appears to be a prominent characteristic of ASPD that is related to the severity of illness and to reduced serotonergic function. Other characteristics of ASPD may confound the specificity of impulsivity. For example, impulsivity has complex potential relationships with education, since either impulsivity or antisocial behavior can interfere with education and education can provide tools to compensate for impulsivity [91]. Impulsivity generally correlates negatively with years of education [5,28]. Presence of ASPD is associated with fewer years of education than comparison groups, but education does not account for effects of ASPD on impulsivity [37].

■ Impulsivity & the course of ASPD

Onset of illness

Current diagnostic criteria for ASPD require early onset [92]. Some individuals have CD that does not persist into adulthood, while others have antisocial behavior with adult onset, potentially secondary to substance abuse [93]. Severe antisocial behavior is generally related to childhood onset of impulsivity [94]; on average, psychopathy in adolescence persists into adulthood [95].

Anxiety and sociopathy would appear to be mutually exclusive but are shared characteristics in ASPD associated with impulsive aggression [96]. The combination of ASPD, anxiety, mood disorders and alcohol dependence may be familial [18].

Relationship with comorbid substance-use disorders

As noted above, two studies showed increased reward-delay impulsivity in addictive disorders if ASPD was present, but the lack of ASPD-only groups precluded studying of the effect of addictive disorder on ASPD [76,97]. Aggressive responding on a human laboratory test [98] and reward-delay impulsivity [99] were not related to cocaine use when presence of ASPD was factored out, although elevated BIS-11 scores persisted. Therefore, comorbid ASPD is an important source of impulsivity in addictive disorders.

Suicidal behavior in ASPD

Rates of suicidal behavior [100] and of completed suicide [101] are increased in ASPD. Comorbid ASPD is associated with increased history of attempted suicide in bipolar disorder [37]. ASPD was associated with increased suicidal behavior in a large clinical population [102]. In some conditions, suicidal behavior was related more to impulsive–aggressive behavior than to depressed mood [103,104]. In 20-year-old men, a suicide attempt during the previous year was associated with aggressive behavior and being a victim of aggression [100]. Impulsive, nearly lethal suicide attempts were not associated with increased depression scores, even though Beck hopelessness scores were increased [105].

■ Summary: impulsivity in ASPD

- Questionnaire-rated and rapid-response impulsivity are increased in ASPD.
- Increased impulsivity in ASPD appears to result from deficient serotonergic function.
- Increased impulsivity in ASPD is associated with increased suicidal behavior.

Combination of bipolar disorder & ASPD

Mechanisms predisposing to impulsivity could cut across bipolar disorder and ASPD, or disorder-specific mechanisms could interact, contributing to behavioral complications of combined bipolar and personality disorders [106]. **Table 2** compares properties and mechanisms of impulsivity in ASPD and bipolar disorder. These results suggest that impulsivity may have different mechanisms in the two disorders.

Personality disorders, including ASPD, may worsen the course of bipolar disorder [3,4,6,7]. There is less information on the effects of concurrent

bipolar disorder on ASPD [8]. Impulsivity could contribute to overlap between bipolar disorder and ASPD [93] by:

- Predisposing jointly to bipolar disorder and ASPD;
- Severe bipolar disorder or ASPD predisposing to comorbid disorders;
- Similar problems in the disorders, but with different mechanisms.

The data in **Table 2** suggest that increased severity of combined bipolar and personality disorders may result from the combination of two different mechanisms of impulsivity.

▪ Bipolar disorder & criminal behavior

Bipolar disorder is characterized by an increased risk for arrest and incarceration [107–109], with higher prevalence among incarcerated individuals than in the community [110,111]. Characteristics of bipolar disorder associated with criminal conviction are summarized in **Table 3**. Psychiatric diagnoses could directly cause increased criminal behavior, or could predispose to it indirectly as a result of comorbid conditions or environmental factors [112]. Over 55% of adolescents with bipolar disorder had juvenile antisocial behavior before their diagnosis [113]. A 13-year prospective study found increased arrests in a nonclinical sample of adolescents with high hypomania scores [114].

A predominately manic course tripled the prevalence of conviction history [115]. In a crime-registry study of subjects discharged from hospitalization for an affective disorder, propensity toward mania predicted subsequent conviction [109]. The number of manic episodes no longer contributed significantly to conviction history when ASPD symptoms and rapid-response impulsivity were taken into account [36].

Rapid-response impulsivity is necessary but not sufficient to increase risk for criminal behavior. ASPD symptom count and rapid-response impulsivity contributed independently to criminal conviction [36]. Impulsivity may interact with factors related to voluntary behavior or earlier experience [116], including:

- Psychopathy [117], consistent with increased, but not borderline, ASPD symptom scores with conviction history [36]. Elements of psychopathy

and impulsivity may cut across ASPD and bipolar disorder and contribute differentially to their severity;

- Childhood trauma [118];
- Substance abuse [109]. In the absence of a substance-use disorder, violent behavior was not increased in bipolar disorder or schizophrenia [119]. In population-based registries of psychiatric hospital discharges and criminal behavior, risk for violent crime in bipolar disorder (n = 3743) versus controls (n = 37,429) was increased only with comorbid substance-use disorder [108].

Conviction was associated with increased suicide attempts; multivariate analysis showed that the only variable significantly associated with suicide attempts in these subjects was total episodes of illness (Wald statistic = 7.3; p = 0.007) [36]. Therefore, the relationship between criminal convictions and past suicidal behavior in bipolar disorder appears largely to result from more severely recurrent illness.

▪ Interactions of ASPD & bipolar disorder

Trait impulsivity

In a study comparing ASPD, bipolar disorder, combined disorder and controls, trait impulsivity (BIS-11 scores) was higher in bipolar disorder than in ASPD (effect size = 0.7) or controls (effect size = 1.4); impulsivity in subjects with ASPD only was higher than in controls (effect size = 0.75) [37]. Psychiatric symptoms (factor scores for depression, mania, anxiety and psychosis) were higher in bipolar disorder alone than ASPD, but were identical in subjects with bipolar disorder regardless of ASPD. Psychiatric symptoms did not account for the effects of ASPD or bipolar disorder on BIS-11 scores. Regardless of bipolar disorder or ASPD, BIS-11 scores were higher if there was a history of an addictive disorder [37].

▪ Course of illness

Onset

In general, onset of bipolar disorder is earlier when it is combined with a substance-use disorder or a cluster B personality disorder, and this early onset is followed by a more recurrent and severe life course [120]. This may be part of a more general pattern of impulsivity in severe childhood-onset psychiatric disorders. Early-onset bipolar disorder is associated with substance-use disorders,

Table 2. Impulsivity mechanisms in antisocial personality disorder and bipolar disorder.

Measure	ASPD	Bipolar disorder (uncomplicated)	Bipolar disorder (complicated or manic)
Questionnaire	↑	↑	↑↑
Rapid-response	↑	↔	↑↑
Reward-delay	↑ or ↔?	↑ or ↔?	↑
Norepinephrine	↔; ↓ sensitivity?	↔; ↑ sensitivity	↑
Serotonin	↓; ↓ sensitivity	↔	↔ or ↓?

↑: Increased compared with controls; ↓: Decreased compared with controls; ↔: Normal; ASPD: Antisocial personality disorder.

ASPD and severe course of illness [121]. Early age at first drink, beyond alcoholism, is associated with a range of disorders related to impulsivity and disinhibition; psychopathology usually predated the first drink [122]. Early onset of fearful panic was associated with increased risk for both bipolar disorder and ASPD [123]. Childhood ‘psychopathic traits’ predicted eventual bipolar disorder [124].

Effects of ASPD on bipolar disorder

In bipolar disorder, comorbid ASPD was associated with a history of suicide attempt, addictive disorder and many episodes, even after taking BIS-11 score, education and age into account [37]. Educational attainment contributed (negatively) to histories of many manic episodes and addictive disorder regardless of whether ASPD was present [37].

Cluster B personality disorder (usually borderline) was associated with poor outcome after a manic episode [4], higher incidence of suicide attempts [6,102] and a ‘difficult’ course of illness [7]. Medically severe suicide attempts were associated with increased lifetime history of aggression regardless of comorbid personality disorders [125]. Prevalence of personality disorders is greater in multipisode than in first-episode bipolar disorder; this could represent a more recurrent form of the illness, or a consequence of previous episodes [126].

Effects of bipolar disorder on ASPD

In ASPD, co-existing bipolar disorder increased the rate of addictive disorders (91 vs 60% with ASPD alone; Fisher exact test = 0.013) and of suicide attempt (Fisher exact test <0.001). BIS-11 score (Wald statistic = 7.2; p = 0.008), but not bipolar disorder, borderline personality disorder, age or education (Wald statistic <1), contributed to these relationships [37]. Therefore, effects of comorbid bipolar disorder on ASPD appear to result from increased impulsivity rather than bipolar disorder *per se*. This is consistent with

results implicating antisocial characteristics and impulsivity in suicidal behavior in personality disorders [127,128].

■ Summary: interactions between ASPD & bipolar disorder relative to impulsivity

- Criminal conviction in bipolar disorder is associated with increased rapid-response impulsivity, severely recurrent course and suicidal behavior. Rapid-response impulsivity and ASPD symptom count (regardless of actual ASPD diagnosis) independently predicted criminal conviction.
- In bipolar disorder, ASPD predicted severe course of illness, presence of substance-use disorder and suicidal behavior. These characteristics were predicted by the presence/severity of ASPD rather than by questionnaire-rated impulsivity.
- In ASPD, bipolar disorder predicted addictive disorders and suicidal behavior. These characteristics were predicted by increased questionnaire-rated impulsivity rather than bipolar disorder.

Conclusion

■ Relationship between the illnesses

ASPD and bipolar disorder each have a prevalence of approximately 3%, so if they were

Table 3. Bipolar disorder and criminal conviction or arrest.

Predictor	Ref.
Early onset	[131]
Many episodes or hospitalizations	[36,132]
Predominately manic episodes	[36,133]
Addictive disorder	[108,109]
Rapid-response impulsivity	[36]
ASPD symptom count	[36]

ASPD: Antisocial personality disorder.

independent, noninteracting conditions, one would expect the combination to be quite rare (0.09%). The prevalence of combined disorders appears much higher than that. Potential explanations are listed in the sections below.

The disorders are mechanistically or genetically related

- For: early age of onset, overlapping early clinical manifestations, evidence for familial associations including coexistence of antisocial and mood disorder characteristics in family and twin studies, similar clinical problems including substance-use disorders and suicidality; approximately 10% of individuals with bipolar disorder have ASPD, which is approximately three-times the expected rate.
- Against: relationships between impulsivity and transmitter function, and reported transmitter abnormalities, differ between ASPD and bipolar disorder; similar clinical symptoms could be produced by different mechanisms.

Similar characteristics in the two disorders have different mechanisms

- For: evidence that impulsivity in bipolar disorder is related to increased catecholaminergic function, while in ASPD it is related to reduced serotonergic function; family study data suggest that CD and bipolar disorder are separate disorders [22].
- Against: substantial proportions of individuals with ASPD or bipolar disorder appear to have both disorders.

Clarification of these mechanisms will require further family/genetic and neurobiological studies of the apparent overlap between bipolar disorder and ASPD. Meanwhile, clinicians should be alert to signs of the combination in either disorder.

Future perspective

Despite substantial advances, including large, well-conducted epidemiological and familial-genetic studies, combined with increasingly sophisticated genetic and neuroimaging methods, true definitions of most important psychiatric disorders do not exist. No objective measure can tell us that someone does, or does

not, have so-called bipolar disorder, or a so-called personality disorder. The more we know about the course and clinical properties of these conditions, the more we see overlap in their behavioral, clinical and developmental characteristics. ASPD is of particular interest because of its apparent similarities to bipolar disorder, and because of the important questions that this raises about prediction of violence and responsibility for actions.

The information reviewed in this paper points out four promising directions:

- Definition of phenotypes that are relevant to real psychiatric problems and that can produce advances in nosology and treatment. Current descriptive diagnostic criteria have been disappointing in terms of predicting the neurobiology or development of specific treatments. When these phenotypes are better defined, they can be explored with genetic, familial, environmental and neurobiological studies;
- Understanding neurobiological mechanisms that occur over the life course. Much current work is focusing on the potential importance of interactions between environmental and internal processes over the course of development, and mechanisms by which they can be influenced by disease processes;
- Adaptations to behavioral deficits or potential imbalances, and what happens when they are compromised. For example, behavioral sensitization to stressors or stimulants can compromise potentially protective serotonergic mechanisms in bipolar disorder or reverse reduced catecholamine system reactivity in ASPD, increasing susceptibility to disinhibition and impulsive behavior;
- Understanding severe behavioral consequences of these illnesses, including suicidal and violent behavior, can lead to better and more disease-specific strategies for the prediction of risk and preventive treatments.

Research in all of these areas is likely to change the manner in which we look at what we today call bipolar disorder and ASPD. What will we call them in 20 years?

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