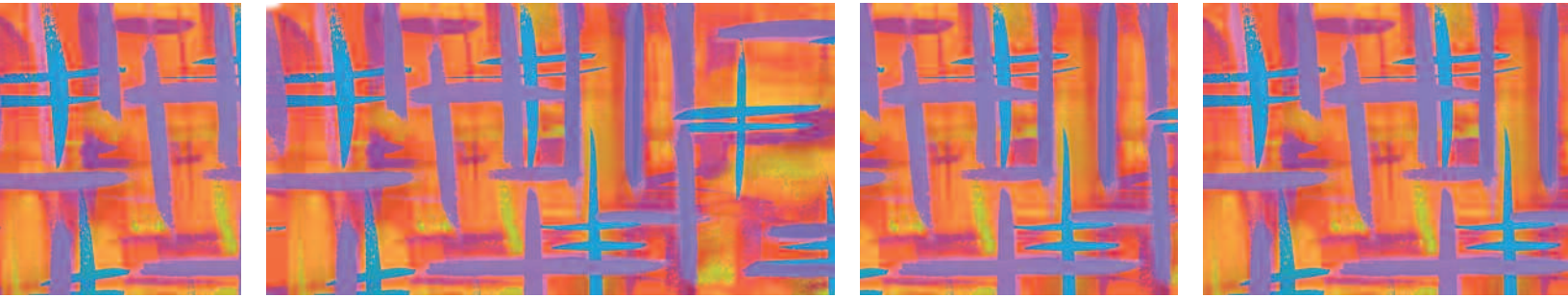


Adult ADHD: Issues and Answers

CME Newsletter of the Adult ADHD Program,
Department of Psychiatry, NYU School of Medicine



Diagnosis: ADHD or Borderline Personality Disorder?

She is in her mid-30s, attractive, and, in her own words, “an incurable romantic.” Since college, she has had 6 jobs and 5 live-in boyfriends. Her jobs invariably end within months after her supervisor tires of her inability to stay focused. Her romantic relationships are equally choppy and always follow the same pattern: falling in love quickly, moving in together within weeks, suddenly disliking her lover, having a series of fights and reconciliations. Then, the boyfriend moves out, and she is despondent and threatens suicide. Explosively angry, she tried to run her last boyfriend down with her car as he was packing his truck to leave. He did not press charges, but she did agree to get some professional help.

While her deficits in impulse control and affect regulation as well as her disturbed interpersonal relationships may lean toward adult attention-deficit/hyperactivity disorder (ADHD), this patient may also have borderline personality disorder (BPD) [see Sidebar: What is BPD?]. A recent review by Philipsen discussed the differential diagnosis and comorbidity of ADHD and BPD in adults.¹ ADHD and BPD have similar clinical features. In addition to the aforementioned deficits, both conditions are also marked by inattention, substance abuse, low self-esteem, and states of aversive inner tension. Yet, differences exist between ADHD and BPD. ADHD patients—the majority being male—regulate their inner tension and affective instability via extreme sports, novelty seeking, and aggression; whereas BPD patients—the majority being female—can behave injuriously in an attempt to end their inner tension.

The symptoms of BPD overlap extensively with ADHD symptoms, specifically as listed in the Utah Criteria for ADHD, which extend *DSM-IV* criteria to include mood regulation symptoms [Tables 1 and 2].^{1,2}

Neurochemical mechanisms

The neurochemical mechanisms by which ADHD and BPD manifest have some similarities. For example, ADHD and BPD are both characterized by impulsivity. Both the serotonergic³ and noradrenergic⁴ systems are posited to be involved in this symptom. Serotonin reuptake inhibitors (SSRIs) have been

Table 1. *DSM-IV* criteria for BPD

A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by 5 or more of the following:

1. Frantic efforts to avoid real or imagined abandonment
2. A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation
3. Identity disturbance: markedly and persistently unstable self-image or sense of self
4. Impulsivity in at least 2 areas that are potentially self-damaging (eg, spending, sex, substance abuse, reckless driving, binge eating)
5. Recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior
6. Affective instability due to a marked reactivity of mood (eg, intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days)
7. Chronic feelings of emptiness
8. Inappropriate, intense anger or difficulty controlling anger (eg, frequent displays of temper, constant anger, recurrent physical fights)
9. Transient, stress-related paranoid ideation or severe dissociative symptoms

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association, 1994;280-281.

shown to reduce impulsivity in BPD.⁵ However, while findings of a potential serotonergic dysfunction in ADHD have been reported,⁶ SSRIs appear to have little or no effect in ADHD other than improving comorbid depression.⁷ In terms of noradrenergic dysfunction, treatment with clonidine, an alpha-2-adrenergic receptor agonist, reduces the impulsivity and hyperactivity of ADHD in children and adolescents and, in a study by Philipsen and colleagues, has decreased aversive inner tension and the urge to commit self-injurious behavior in patients with BPD.⁸ Increased levels of noradrenaline may be

Statement of Need

It is now recognized that attention-deficit/hyperactivity disorder (ADHD), once thought to occur only in children, persists into adulthood in up to 60% of cases. Most adults with ADHD have not been properly diagnosed or treated. Differing patterns of comorbidity and symptom heterogeneity pose new conceptual, diagnostic, and treatment challenges. Accurate diagnosis requires careful consideration of other psychiatric and medical disorders that may mimic the symptoms of ADHD. The majority of patients exhibit at least 1 comorbid psychiatric disorder, such as a major depressive disorder, an anxiety disorder, a personality disorder, a substance abuse disorder, or bipolar disorder. Stimulants and noradrenergic and dopaminergic antidepressants have been shown to be useful medical interventions for adult ADHD. This newsletter will explore conditions comorbid to ADHD in adults and examine the issues involved in diagnosing and treating both the ADHD and the comorbidity.

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Learning Objectives

After completing this activity, you should be better able to:

- Identify the differences between ADHD and borderline personality disorder (BPD)
- Discuss the history and incidence of BPD
- Evaluate the current treatment options for ADHD with comorbidities

Method of Participation

Read this newsletter, complete the CME Posttest Answer Form and Activity Evaluation Form, and fax or mail the forms to Medical Education Resources, Inc. at the address listed. You will receive a certificate by fax or mail. There is no certificate processing fee.

Intended Audience

This activity was developed for psychiatrists, primary care physicians/internists, neurologists, and psychologists.

Effective Dates

Released: February 2007
Expires: January 31, 2008

Accreditation/Designation Statements

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Medical Education Resources, Inc. and MedLearning Inc. Medical Education Resources, Inc. is accredited by the ACCME to provide continuing medical education for physicians.

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Faculty Author

Lenard A. Adler, MD
Director, Adult ADHD Program
Associate Professor
Departments of Psychiatry and Neurology
New York University School of Medicine
New York, New York

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Dr Adler has received honoraria from Medical Education Resources, Inc. for his assistance as editor. In addition, he has disclosed the following relevant financial relationships:

Dr Adler receives grant/research support from Abbott Laboratories, Bristol-Myers Squibb Company, Cortex Pharmaceuticals, Inc., Eli Lilly and Company, Johnson & Johnson, McNeil Consumer and Specialty Pharmaceuticals, Merck & Co., Inc., Novartis Pharmaceuticals, Pfizer Inc. and Shire US Inc. He is a consultant for Abbott Laboratories, Bristol-Myers Squibb Company, Cephalon Inc., Cortex Pharmaceuticals, Inc., Eli Lilly and Company, Johnson & Johnson, McNeil Consumer and Specialty Pharmaceuticals, Merck & Co., Inc., Novartis Pharmaceuticals, Pfizer Inc. and Shire US Inc. Dr Adler has participated in speakers' bureaus for Eli Lilly and Company, Johnson & Johnson, McNeil Consumer and Specialty Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Inc. and Shire US Inc.

The staff of Medical Education Resources, Inc. has nothing to disclose.

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Use of Brand and Generic Names

Brand names of products for treating attention-deficit/hyperactivity disorder (ADHD) are used throughout this continuing medical education (CME) activity so that participants can distinguish among the many different formulations (duration of action, delivery system) of products with the same generic name.

Unlabeled Use Disclosure Statement

Participants are advised that this CME activity will contain references to unlabeled/unapproved/investigational uses of drugs to treat ADHD.

Disclaimer

The opinions expressed in this activity are those of the author and do not necessarily reflect those of Medical Education Resources, Inc., MedLearning Inc., or Shire. Please consult the appropriate package insert for full prescribing information on all drug therapies discussed.

Table 2. Utah Criteria for ADHD in adults overlapping with BPD symptoms

1. Childhood history consistent with ADHD is required, dating back to at least age 7.
2. Adult symptoms:
 - a. Hyperactivity and poor concentration should be present in adulthood
 - b. In addition, 2 of the following symptoms are required:
 - Affective lability
 - Hot temper
 - Inability to complete tasks and disorganization
 - Stress intolerance
 - Impulsivity

Philipsen A. Differential diagnosis and comorbidity of attention-deficit/hyperactivity disorder (ADHD) and borderline personality disorder (BPD) in adults. *Eur Arch Psychiatry Clin Neurosci*. 2006;256(Suppl 1):i42-i46.

related to the cognitive and antidepressant effects of the atypical antipsychotic drugs.⁹ Based on that premise, a recent study suggested that quetiapine may be effective for the treatment of some BPD characteristics, including low mood and aggression.¹⁰ Increased levels of noradrenaline may be related to the cognitive and antidepressant effects of the atypical antipsychotic drugs.⁹ Because of their impact on the noradrenergic system, other drugs may become useful in BPD. For example, the tricyclic antidepressant desipramine,¹¹ the aminoketone antidepressant bupropion,¹² and the nonstimulant atomoxetine,¹³ all of which inhibit the reuptake of norepinephrine to some extent, and which have been used to control ADHD symptoms may become viable therapeutic options for such BPD patients with comorbid ADHD. Amphetamine-type psychostimulants release norepinephrine more potently than they release dopamine and serotonin,¹⁴ and these agents may be a pharmacologically rational route for therapy.

Joyce and colleagues found that a dopamine transporter polymorphism is a risk factor for BPD in depressed patients and contributes to a poorer prognosis in patients with this abnormality.¹⁵ In ADHD, a dopaminergic dysfunction is the crucial neurochemical mechanism of attention deficit,¹⁶ and may explain some of the overlapping characteristics of ADHD and BPD. Because no blood tests, physical examination findings, or imaging studies can offer any indicative information, the diagnosis of BPD rests upon the correlation of *DSM-IV* characteristics with the patient's symptoms.

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What is BPD?

BPD is a serious psychiatric condition characterized by pervasive instability in moods, interpersonal relationships, self-image, and behavior. This instability often disrupts family and work life, long-term planning, and the individual's sense of self-identity. Originally thought to be at the brink of psychosis, individuals with BPD experience instead a disorder of emotion regulation. While less well known than schizophrenia or bipolar disorder, BPD is more common, affecting 2% of adults, mostly young women.¹ A high rate of self-injury without suicide intent has been observed, as well as a significant rate of suicide attempts and completed suicide in severe cases.² Patients often need extensive health services. For example, one study showed that nonremitted BPD patients were found to be significantly less likely than remitted BPD patients to have a history of a syndrome-like condition (ie, chronic fatigue, fibromyalgia; $P < .05$), more likely to smoke ($P = .002$), drink alcohol ($P = .003$), and use sleep medications ($P < .001$) or chronic pain medications ($P = .03$).³

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Case study—Woman presents with BPD, ADHD, and depression

A 35-year-old woman presents for evaluation for chronic depressed mood, of which she has had a continuous history more or less since middle school. She has no clear vegetative symptoms of depression (insomnia, anorexia, decreased libido), and her mood tends to brighten when she does things she enjoys and is with others who are enjoying themselves. She has been in psychotherapy intermittently for the last decade, with little success. She feels that therapists do not “get” her depression, and states she always feels “empty.” Treatment with multiple SSRIs has been ineffective and each led to decreased libido. She has a history of marijuana use and has tried cocaine. She also smokes a pack per day and feels anxious when she tries to quit.

She has a spotty relationship history with multiple boyfriends, often fights with her friends, and ends relationships when she perceives being wronged. She has also had numerous jobs which she changes quickly when she feels things are not going her way, blaming her employer. When angry, she has been known to throw things in her apartment. She has made 2 impulsive suicide gestures—a superficial wrist slash and ingesting 5 fluoxetine 20-mg capsules—and immediately called her therapist after each attempt. She denies clear symptoms of mania, without grandiosity and entitlement, although intermittently impulsively spends.

In terms of ADHD, she had an onset of hyperactivity at the age of 7, with her second-grade report card noting talking out of turn and being in and out of her chair. Current symptoms include significant inattention (trouble remembering what is read or said), easy distraction, misplacing items, trouble with deadlines, trouble planning, drifting in conversations, restlessness and need to regularly exercise, feeling revved up at night, talking out of turn, impulsively buying items, interrupting others when busy, and difficulty waiting. Reviews at work have noted her inability to follow through an assignment or task, as well as trouble with deadlines and tardiness. Her current psychiatrist has diagnosed her with BPD, ADHD, and dysthymia.

Treatment plan

The key here is to use a combination of psychotherapy and medication. Given her history of substance use, including cigarette smoking, bupropion XL was used to treat the ADHD, depression, and smoking; psychostimulants and atomoxetine were rejected because of her history of substance abuse, depression, and impulsivity. It was decided to titrate the bupropion slowly because of the patient's reported sensitivity to side effects in prior medication trials. Finally at a dose of 300 mg/d, an improvement in mood and attention was noted with decreased restlessness, distraction, and impulsivity. Her cigarette smoking was also decreased by 50%. She has ongoing issues with rejection sensitivity and continues to work in psychotherapy.

Combining psychotropic drugs can be safe if risks are monitored

When combining medications, clinicians must consider the possible interactions among the therapeutic agents. Patients should be monitored carefully for adverse effects and possible concomitant cardiovascular effects of combining medications with stimulants or atomoxetine. Instruct patients to be aware of any physical or mental changes that may occur at the initiation of new therapies as well. Preliminary research on drug-drug interactions indicates that combining medications can be done safely. For example, Cohen and colleagues describe a chart review of 142 children and adolescents, 29 of whom were coadministered desipramine, a tricyclic antidepressant, and a stimulant medication (methylphenidate [MPH] or dextroamphetamine).¹ The combination of desipramine and either stimulant did not produce any statistically or clinically significant interaction. Wilens et al, who compared individual and combined treatment with OROS-MPH and atomoxetine, revealed that a greater number of adverse events occurred with the combination but that they were generally tolerable.² Adler and coworkers, who examined the combination of atomoxetine and stimulants in a chart review, also found that most side effects were tolerable.³ A review by Markowitz and colleagues of 38 reports involving 25 different drugs from various classes that specifically assessed psychotropic drug interactions concluded that although current research is limited, the existing data indicate that stimulants can be used concomitantly with most classes of medications with the exception of monoamine oxidase inhibitors.⁴ This research on drug-drug interactions is limited mostly to children and adolescents. A complete understanding of these interactions is required before combination pharmacotherapy can be generally recommended to adults, some of whom may be taking nonpsychotropic medications for chronic conditions such as hypercholesterolemia or diabetes.

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Journal reviews

Pilot study of OROS-MPH improves core symptoms and deficits in executive function in adults

OROS-MPH was the first extended-release formulation of MPH designed with the aim of providing true once-a-day stimulant therapy for ADHD.¹ An open-label uncontrolled 38-day study evaluated its effectiveness in improving core symptoms and deficits in executive function of adults with *DSM-IV*-defined ADHD.² Eligible patients required a baseline Conners' Adult ADHD Rating Scale (CAARS) score ≥ 24 and a Clinical Global Impression of Severity (CGI-S) score ≥ 4 (at least moderate illness). The primary end point of efficacy was a change in CAARS scores; secondary effectiveness parameters included executive function. Neither adverse events of a serious nature nor early withdrawals due to adverse events were reported. Mean pulse rate increased by 5.9 beats/min ($P=.003$) and mean body weight decreased by 2.2 kg (1 lb) at end point ($P<.0001$). Both total CAARS scores as well as the inattention and hyperactivity/impulsivity symptom subscales decreased significantly at end point ($P<.0001$ for both comparisons). Statistically significant improvements were observed in executive function and all other secondary measures, including the CAARS self-report. The modal dose of OROS-MPH was 54 mg. This trial suggests that OROS-MPH is well tolerated, providing improvements in executive function. Larger, randomized, controlled studies are needed to confirm these results.

PCPs prefer to refer possible ADHD patients

Most primary care physicians (PCPs) would rather refer patients with possible adult ADHD to a specialist, says a study presented by the 2006 American Psychiatric Association Annual Meeting.³ A Harris Interactive online survey of 400 PCPs found that about 2 out of 3 PCPs (65%) were uncomfortable making a diagnosis of ADHD without referral to a specialist, compared to 2% who would refer for depression, and 3% who would refer for generalized anxiety disorder. A scant 5% of survey respondents reported that they would decide to treat their adult ADHD patients with medication. Most of the PCPs surveyed (85%) said they would take a more active role in diagnosing and treating adult ADHD if they had an easy-to-use screening tool. Assessment tools that can be used in the primary care arena can be found at www.med.nyu.edu/psych/psychiatrist/adhd.html.

MPH treats some—but not all—attentional deficits

A study by Tucha and colleagues examined the effect of MPH on attentional functioning of adults with ADHD.⁴ Sixteen adults with diagnosed ADHD without comorbidity as well as 16 healthy participants were assessed twice: at baseline prior to MPH initiation and following MPH treatment. The assessment battery consisted of reaction time tasks of low complexity, including measures of alertness (subdivided into tonic and phasic alertness), vigilance, divided attention, flexibility, and aspects of selective attention including focused attention,

inhibition, and integration of sensory information. The results suggest that adults with ADHD who are not on stimulant medication are impaired in various components of attention and executive function, including vigilance, divided attention, selective attention, and flexibility. Conversely, treatment of adults with ADHD using individually tailored doses of MPH has a positive effect on measures of alertness, vigilance, selective attention, divided attention, and flexibility. However, even with MPH treatment, adults with ADHD displayed considerable deficits in vigilance and integration of sensory information. These findings imply that adults with ADHD are not differentially impaired in attentional processes and executive functioning, but may suffer from a more global deficit of attention. Although MPH treatment has been found to be effective in the treatment of the attention deficit of adults with ADHD, additional treatment appears to be necessary to control all attentional functioning deficits. However, because only a minority (31%) of adults with ADHD appear to have deficits in executive functioning,⁵ caution must be taken not to place the patient on additional medication until such symptoms have been documented.

ADHD drug adherence rates can drop over time, patient education needed

Recent evidence shows that, although patients may continue their ADHD medication for several months following initiation, they do not consistently take medication for more than 2 months.⁶ Given these treatment patterns, pharmacologic treatment in newly treated ADHD patients may be suboptimal and may impact outcomes. A study published in 2006 analyzed pharmacy database records cataloging filled prescriptions for psychostimulants, antidiabetes agents, and lipid-normalizing drugs (statins) from the fall of 2003 through the fall of 2004.⁷ Subjects entering the observation period had filled a prescription for the first time in 90 days. Subjects were considered persistent with a medication at a given time point when the current fill date was within 2 months of the previous fill date. By month 2 of the observation period, adherence rates were similar for psychostimulants, antidiabetic agents, and statins. By month 7, adherence rates for mixed amphetamine salts extended release (23%) and MPH modified release (24%) were similarly low, whereas refill rates were slightly higher for rosiglitazone (an antidiabetic agent) (33%) and the statins (26-30%), and similar or slightly lower for insulin treatments (18% for insulin glargine). Conclusions from this study should be viewed cautiously because diagnostic indications for the therapeutic treatment were not examined. However, this study suggests, from a pharmacy claims perspective, that adherence to long-acting stimulant agents may be similar to adherence to treatments for other chronic illnesses. Because patients must go through individualized dosing changes of their stimulant medication, the patient may decide to discontinue the drug if symptoms are not controlled in a timely fashion. The result is a failed clinical outcome. Thus, more patient education is needed for adult ADHD patients who must be vigilant in reporting any shortfalls in their therapy to their physician.

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Posttest

Please select only 1 answer for each question. Circle the letter corresponding to the correct answer on the answer form on the next page.

- Which statement is true about the differences between ADHD and BPD?
 - The majority of patients with BPD are male
 - Patients with ADHD tend to regulate their inner tension and affective instability via extreme sports, novelty seeking, and aggression
 - The majority of patients with ADHD are female
 - Patients with ADHD tend to inflict self-injuries in an attempt to end their inner tension
- All but which of the following is a Utah criterion for ADHD in adults overlapping with BPD symptoms:
 - Childhood history consistent with ADHD, dating back to at least age 13
 - Hot temper
 - Impulsivity
 - Stress intolerance
- A study by Philipson and colleagues showed that treatment with which drug corrected some of the noradrenergic dysfunction that presented as aversive inner tension and self-injurious behavior associated with BPD?
 - Atomoxetine
 - MPH
 - Clonidine
 - Desipramine
- A recent study by Perella et al examined which atypical antipsychotic for the treatment of some BPD characteristics, including low mood and aggression?
 - Ziprasidone
 - Quetiapine
 - Aripiprazole
 - Risperdone
- BPD was once believed to be at the brink of:
 - Paranoia
 - Bipolar disorder
 - Schizophrenia
 - Psychosis
- What is true about the incidence of BPD?
 - It is less common than schizophrenia
 - It is more common than bipolar disorder
 - Like ADHD, it mainly affects males
 - It affects about 10% of adults
- The existing data indicate that psychostimulants can be used concomitantly with most classes of medications, with the exception of:
 - HMG-CoA reductase inhibitors
 - Azole antifungals
 - Protease inhibitors
 - Monoamine oxidase inhibitors
- A Harris Interactive online survey found that PCPs were most comfortable making a diagnosis of:
 - ADHD
 - Depression
 - Generalized anxiety disorder
 - A and C
- A study by Tucha showed that treatment of adult ADHD with MPH has a positive effect on all but the following measures:
 - Integration of sensory information
 - Alertness
 - Selective attention
 - Divided attention
- Recent evidence shows that ADHD patients do not consistently take medication for more than:
 - 2 months
 - 4 months
 - 6 months
 - 12 months

Adult ADHD: Issues and Answers

Successful completion of the posttest examination (at least 70% correct) and activity evaluation is required to earn a maximum of .75 AMA PRA Category I Credits™. Statements of Credit will be awarded upon successful completion of the posttest and evaluation.

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Posttest Answer Form	
(Circle the correct answer to each question)	
1. A B C D	6. A B C D
2. A B C D	7. A B C D
3. A B C D	8. A B C D
4. A B C D	9. A B C D
5. A B C D	10. A B C D

To receive credit, you must answer 7 of the 10 posttest questions correctly, complete all forms, and submit them by January 31, 2008.

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I certify that I have completed this CME activity. The actual amount of time I spent on this activity was _____ minutes.

Signature _____ Date _____

Activity Evaluation Form

Please circle the appropriate rating in answer to the questions that follow:

- How would you rate the content of this CME activity?
 Poor 1 2 3 4 5 Outstanding
- How relevant was the content of this activity to your practice?
 Not relevant at all 1 2 3 4 5 Very relevant
- To what degree were you able to meet each of the learning objectives of the activity? Please respond to each learning objective listed below:
 - Identify the differences between ADHD and borderline personality disorder (BPD)
 Poor 1 2 3 4 5 Outstanding
 - Discuss the history and incidence of BPD
 Poor 1 2 3 4 5 Outstanding
 - Evaluate the current treatment options for ADHD with comorbidities
 Poor 1 2 3 4 5 Outstanding
- Based on your knowledge and experiences, the level of the activity was:
 Basic Appropriate Complex
- How would you rate the activity overall?
 Poor 1 2 3 4 5 Outstanding
- Do you believe this activity was fair, balanced, and free of commercial bias?
 - Yes No
 - If No, please state the reason:

- How much did this activity enforce your current clinical opinions?
 Not at all 1 2 3 4 5 A lot
- How much new information did you find in this activity?
 None 1 2 3 4 5 A lot
- As a result of this activity, will you alter your practice?
 Yes No
- If Yes, please describe any change(s) you plan to make:

- How committed are you to making these changes?
 Not at all committed 1 2 3 4 5 Very committed
- If No, why not? _____
- Additional comments about this activity?

- Do you feel future activities on this subject matter are necessary and/or important to your practice?
 Yes No
- Please list any other topics that would be of interest to you for future educational activities.




Adult ADHD: Issues and Answers

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MedLearning Inc.
611 Route 46 West
Hasbrouck Heights, NJ 07604

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