Managing Aggressive Behavior in Patients With Obsessive-Compulsive Disorder and Borderline Personality Disorder

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Obsessive-compulsive disorder (OCD) is one of the most common psychiatric disorders, occurring in 2% to 3% of the U.S. population. Borderline personality disorder is found in 2% of the U.S. population. These disorders denote the endpoints on a spectrum of compulsive and impulsive disorders. One endpoint marks compulsive or risk-aversive behaviors characterized by overestimation of the probability of future harm, highlighted by OCD. The other endpoint designates impulsive action characterized by the lack of complete consideration of the negative results of such behavior, such as borderline and antisocial personality disorders. This article examines studies testing the efficacy of different medications in treating compulsive and impulsive disorders. Mood stabilizers such as divalproex, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and neuroleptics have documented efficacy in treating aggression and affective instability in impulsive patients.

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Anger and aggression are not generally associated with obsessive-compulsive disorder (OCD), one of the most common psychiatric disorders affecting 2% to 3% of the U.S. population.1 Anger and aggression frequently accompany borderline personality disorder, however. Nevertheless, a careful consideration of both these disorders reveals that anger and aggression are characteristics linking OCD to borderline personality disorder.

OCD is generally characterized by anxiety-provoking and intrusive thoughts (such as fear of contamination or germs, doubt and uncertainty about future harm, and the need for symmetry) and by repetitive behaviors (such as constant checking, washing, touching, and counting). Though anger is not a key feature of OCD, it is associated with specific subtypes and certain comorbid conditions.2 Patients who are hoarders, for example, may respond with anger and aggression when hoarded objects are taken from them. Another unique subgroup that manifests impulsive aggression or anger are those OCD patients with comorbid tics and attention-deficit/hyperactivity disorder (ADHD). Patients with Tourette’s disorder and tic-related OCD symptoms often have comorbid ADHD with impulsivity and aggression. Agitation, anger, and aggression in some OCD patients can also be related to comorbid obsessive-compulsive spectrum disorders. Patients with other neurologically based disorders—including pervasive developmental disorders like autism—who present with many repetitive behaviors, can also have high levels of impulsivity and aggression. In some impulse-control disorders, such as repetitive self-mutilation, self-directed aggression is an important concern.

OBSESSIVE-COMPULSIVE SPECTRUM

Anger and aggression are found across the obsessive-compulsive spectrum, a group of disorders also characterized by intrusive thoughts and by repetitive behaviors. These OCD spectrum disorders may share other characteristics with OCD, such as age at onset, clinical course, and family history.3 OCD spectrum disorders may affect up to 10% of the U.S. population.4 My colleagues and I have focused on 3 symptom clusters within the OCD spectrum: disorders characterized by preoccupation with bodily sensations or appearance such as body dysmorphic disorder and hypochondriasis, depersonalization, and eating disorders such as anorexia; impulse control disorders such as trichotillomania, pathological gambling, and sexual compulsions; and neurologic disorders such as Tourette’s disorder, Sydenham’s chorea, and autism (Figure 1).

If these disorders are categorized according to estimations of risk and placed on a dimensional linear spectrum, one endpoint will mark compulsive or risk-aversive behaviors characterized by overestimation of the probability of future harm. The other endpoint will designate impulsive...
Figure 1. Obsessive-Compulsive–Related Disorders

- Preoccupations with bodily sensations or appearance
- Body dysmorphic disorder
- Depersonalization
- Hypochondriasis
- Anorexia nervosa
- OCD
- Obsessions with thoughts and impulses
- Sexual compulsions
- Trichotillomania
- Pathological gambling
- Kleptomania
- Self-injurious behavior
- Tourette’s disorder
- Sydenham’s chorea
- Neurologic disorders
- Torticollis chorea

Comorbidity

Many patients with OCD also have other psychiatric disorders. My colleagues and I analyzed data from the National Institute of Mental Health Epidemiologic Catchment Area (ECA) study, comparing subjects with uncomplicated OCD (without history of any other lifetime psychiatric disorder), comorbid OCD (with any other lifetime psychiatric disorder), other lifetime psychiatric disorders, and without lifetime psychiatric disorders. We found that 140 of 18,325 respondents met criteria for uncomplicated OCD, while 266 met criteria for comorbid OCD. The persons with comorbid OCD also commonly had anxiety disorders such as agoraphobia at a rate of 39%, social phobia at a rate of 19%, and panic disorder at a rate of 14%; substance use disorders including alcohol abuse/dependence at a rate of 34% and drug abuse/dependence at a rate of 22%; and affective disorders such as major depression at a rate of 32%, dysthymia at a rate of 26%, and bipolar disorder at a rate of 10%. Comorbid OCD was twice as prevalent as uncomplicated OCD in the sample.

Treatment

Serotonin dysfunction has long been linked to OCD as well as impulsive aggressive behavior. Selective serotonin reuptake inhibitors (SSRIs) are currently the treatment of choice for OCD. The response to medication is seldom immediate, but once established, it is usually maintained. At the impulsive end of the spectrum, conversely, there is often a rapid response in patients treated with SSRIs and good results in short-term trials. However, some patients (those with trichotillomania, in particular) lose their response over time. It has been suggested that this failure to maintain a response may occur in patients with other impulsive personality disorders as well.

If patients are unresponsive to SSRIs, the physician should augment the original medication. Treatment augmentation in patients with OCD should be guided by the subtype or comorbid condition of this disorder. For example, since ADHD patients respond favorably to stimulants, OCD patients with comorbid ADHD should have the initial SSRI medication augmented with stimulants. Similarly, patients with bipolar illness respond to mood stabilizers. Thus in OCD patients with comorbid bipolar illness, one might augment SSRIs with a mood stabilizer.

OCD patients with EEG abnormalities—particularly those who show excess theta activity in frontal areas—may respond well to a mood stabilizer or anticonvulsant. These patients are generally less responsive to serotonin reuptake inhibitors and may be more responsive to mood stabilizers or to anticonvulsants like divalproex. Divalproex may also prove effective in patients with EEG abnormalities including seizure disorders and neurologic soft signs.

BORDERLINE PERSONALITY DISORDER

Borderline personality disorder, which is at the impulsive end of the compulsive and impulsive spectrum, is a common diagnosis, occurring in 2% of the U.S. population, 10% of the outpatient population, and 20% of the inpatient population; almost half of other personality disorder patients also have comorbid borderline personality disorder.
disorder. Associated with high rates of morbidity and mortality, this illness is chronic and debilitating. DSM-IV categorizes borderline personality disorder as “an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual’s culture, is pervasive and inflexible, has an onset in adolescence or early adulthood, is stable over time, and leads to distress or impairment.” Datenschutz Borderline personality disorder is defined in DSM-IV as “a pattern of instability in interpersonal relationships, self-image, and affects, and marked impulsivity.” DSM-IV criteria include impulsivity in at least 2 different areas that are potentially self-damaging: spending, sex, substance abuse, reckless driving, binge eating, and recurrent suicidal behavior or gestures. They also include “affective instability due to a marked reactivity of mood.” Inappropriate, intense anger, or difficulty controlling anger (e.g., frequent displays of temper, constant anger, or recurrent physical fights) are also included among the criteria. The inappropriate expression of anger is a key feature of borderline personality disorder.

Fyer et al. conducted a retrospective chart review of 180 patients who met DSM-III criteria for borderline personality disorder. Ninety-one percent of the patients reviewed had one other diagnosis, and 42% percent had 2 or more comorbid diagnoses. They found that no comorbid disorder occurred more frequently in patients with borderline personality disorder than another—affective disorders, schizotypal and psychotic disorders, organic disorders, substance dependence, and other personality disorders appeared with the same frequency.

Due to the high rate of comorbidity, a differential diagnosis is very important in the identification of borderline personality disorder; it can be mistaken for mood-related disorders, other personality disorders, or medical contributing factors. The core symptoms of the disorder—impulsivity and aggression—contribute to major public health problems such as violence, motor vehicle accidents, substance abuse, and suicide. Clinicians should decide whether they want to target specific clinical symptoms or dimensions or broader, more nonspecific effects in treating patients with borderline personality disorder. Cowdry and Gardner have noted that borderline personality disorder offers a diverse array of target symptoms for pharmacotherapy, including affective symptoms such as depression, anxiety, rage, and dysphorias; cognitive disturbances such as brief psychotic episodes or interpretative distortion; and impulsive, self-injurious behaviors. An association between borderline personality disorder and a number of psychiatric disorders that are responsive to medication has been suggested. Among them are border personality disorder and DSM-III Axis I major affective disorders, hysteroid (rejection-sensitive) dysphoria (which may respond to monoamine oxidase inhibitors [MAOIs]), ADHD, neurologic injury, and epileptoid disorders.

**Treatment**

A broad range of different medications has been used, mostly in small, controlled studies of various diagnostic precursors of borderline personality—emotionally unstable character disorder, a broad range of personality disorders—and borderline personality disorder. Neuroleptics have had some role. Antidepressants have been used but have been associated with an increase in anger in some cases. Mood-stabilizing medicines like lithium and anticonvulsants like phenytoin have been shown to be helpful for hostility, emotional instability, and aggression.

A better understanding of the neurobiology of borderline personality disorder may help in selecting treatment approaches. Biological challenges with serotonin agonists such as m-chlorophenylpiperazine (m-CPP) have elicited informative behavioral responses. One subgroup of patients responded with disinhibition; another experienced a depersonalized or LSD-like experience—core symptoms of borderline personality disorder. In terms of the endocrine response, patients have shown both an increased cortisol response, unique to this population, and a blunted
The medications currently used to treat borderline personality disorder include antipsychotics, SSRIs, the MAOI phenelzine, and anticonvulsants like carbamazepine and divalproex.

**Antipsychotics.** Goldberg et al. found the antipsychotic thiothixene to be useful for targeted symptoms in the treatment of patients who met DSM-III criteria for borderline personality disorder, schizotypal personality disorder, or both. In this 5-week placebo-controlled trial, 50 patients received doses of thiothixene lower than those given to outpatients with schizophrenia. (The mean daily dose of thiothixene during the final week of the trial was 8.7 mg/day.) The Schedule for Interviewing Borderlines, the Global Assessment Scale (GAS), a 100-point scale rating functioning, and the Hopkins Symptom Checklist (SCL-90) were used to assess patient response. Although the researchers found no drug effect on patients’ total borderline, schizotypal, or GAS scores, thiothixene proved significantly superior to placebo on measures of illusions (p = .0001), ideas of reference (p = .0140), psychoticism (p = .0001), obsessive-compulsive symptoms (p = .0321), and phobic anxiety (p = .0005) in all patients, regardless of their diagnosis. The authors argue for a subdiagnosis based on symptoms that are drug-responsive, not all of which are found in current diagnostic criteria.

In a double-blind, longitudinal crossover study, Cowdry and Gardner compared placebo with an MAOI, tranylcypromine, as well as a high-potency benzodiazepine, alprazolam; an anticonvulsant, carbamazepine; and a neuroleptic, trifluoperazine. Sixteen female outpatients with borderline personality disorder and prominent behavioral dyscontrol but who were not experiencing a current episode of major depressive disorder comprised the study cohort. An interesting finding was that episodic dyscontrol increased in patients taking alprazolam. A modified Bunney-Hamburg scale measured the average degree of depression, anxiety, anger, loneliness, feelings of rejection, sense of unreality, and euphoria and was used to obtain ratings from both physician and patients. In addition, a 7-point scale similar to the Clinical Global Impressions scale (CGI) was used to obtain ratings of clinical change at the end of each trial. Changes in behavioral dyscontrol were evaluated by asking patients and physicians to note instances of angry outbursts, physical violence toward objects or toward people, self-damaging acts, and suicide threats, gestures, and attempts. Patients who were able to tolerate a full trial of trifluoperazine showed improvement.

**SSRIs.** The incidence of self-mutilative episodes decreased significantly in a group of patients treated with fluoxetine. Markovitz et al. conducted a prospective, nonblind trial of fluoxetine in the treatment of 22 outpatients who met DSM-III-R criteria for borderline personality disorder (N = 8), schizotypal personality disorder (N = 4), or both (N = 10). Fluoxetine was begun at 20 mg/day and increased in 20-mg/day increments each third day to a maximum of 80 mg/day. At 3, 6, 9, and 12 weeks, results were evaluated by comparing patient reports of self-mutilation and the SCL-90. At week 9, 50% fewer patients reported self-injuries, and the number of mutilative episodes had decreased by 74%. At week 12, only 2 patients continued these acts of self-mutilation, at a rate of less than once a week. At week 12, the mean SCL-90 score had lowered (improved) significantly (p < .001) compared with baseline.

Kavoussi et al., noting the biological studies suggesting that impulsive, aggressive, and self-destructive behaviors in borderline personality disorder are accompanied by abnormal CNS serotonergic functioning, conducted an 8-week, open trial of the SSRI sertraline in 11 patients meeting DSM-III-R criteria for at least one personality disorder. Impulsive-aggressive behavior and irritability were measured with the Overt Aggression Scale-Modified for Outpatients (OAS-M) at baseline, week 2, 4, and 8. Seven of 11 patients completed the 8-week trial, while 9 completed at least 4 weeks of treatment. Significant changes from baseline on measures of aggression (p = .05) appeared by week 2 and on irritability (p = .05) by the end of week 4; this improvement continued through week 8. The authors stress that controlled studies with larger patient populations are necessary, but note that these results support the hypothesis that different biological substrates are responsible for different symptoms and personality traits in patients with personality disorder and that these patients show a differential response to pharmacologic therapies with specific modes of action.

Coccaro and Kavoussi addressed the specific area of impulsive-aggressive behavior and irritability in 40 outpatients with personality disorders including 13 with borderline personality disorder. They conducted a 12-week, double-blind, placebo-controlled study of fluoxetine in these outpatients, all of whom met DSM-III-R criteria for either Axis I or II personality disorder with a history of impulsive-aggressive behavior and irritability. Patients were administered 20 mg/day of fluoxetine for the first 4 weeks of the study, when the dosage could be raised to 40 mg/day and to 60 mg/day after week 8. The primary scales for outcome assessment were the OAS-M and the CGI-Improvement subscale (CGI-I), a 7-point global change scale indicating improvement by scores of 1 (very much improved) or 2 (much improved). CGI-I scores of 1 or 2 were counted as response. The proportion of fluoxetine-treated patients responding was always greater than the proportion of placebo-treated patients responding, and the difference was statistically significant (p = .03) at weeks 4, 8, 12, and endpoint. Patients treated with fluoxetine also recorded scores on the OAS-M Aggression subscale that were significantly lower (improved) than those of placebo-treated patients at weeks 10 (p = .02) and 12.
(p = .01). Significantly lower scores on the OAS-M Irritation subscale were recorded by fluoxetine-treated patients compared to those recorded by placebo-treated patients at weeks 6 (p = .02), 8 (p = .02), 10 (p = .006), and endpoint (p = .01). Patients with DSM-III-R personality disorders showed an anti-aggressive effect when treated with fluoxetine compared with placebo-treated patients. The authors seem to imply that patients who respond to SSRIs achieve a sustained response to the agent.

**MAOIs.** Soloff et al. compared the efficacy of the MAOI phenelzine with the neuroleptic haloperidol and placebo against the affective, cognitive, and impulsive-aggressive symptoms of borderline personality disorder in 108 outpatients and suggested that phenelzine may be useful for treating self-directed anger and hostility in patients with borderline personality disorder. In this 5-week trial, the researchers attempted to differentiate affective from schizotypal symptoms in this patient population with borderline personality disorder. Noting that placebo effects are “powerful and specific,” Soloff et al. acknowledged the difficulties of treating acute symptoms of borderline personality disorder with pharmacotherapy alone. On measures of depression, borderline psychopathologic symptoms, and anxiety, phenelzine was superior to placebo in these patients. The researchers were unable to replicate the superior efficacy of a neuroleptic; they found phenelzine superior to haloperidol, as well. Phenelzine also proved significantly (p < .001) superior to placebo in treating patients’ anger and hostility. Soloff and colleagues suggest a new indication for phenelzine in treating the borderline personality disorder patient’s self-perceived anger and hostility.

Physicians rated patients taking carbamazepine (p < .01) and tranylcypromine (p < .05) as significantly improved compared with those taking a placebo, while patients rated themselves as significantly (p < .001) superior to placebo in treating patients’ anger and hostility. Soloff and colleagues suggest a new indication for phenelzine in treating the borderline personality disorder patient’s self-perceived anger and hostility.

**Anticonvulsants.** Cowdry and Gardner’s suggestion that carbamazepine—an anticonvulsant—might be helpful in treating aggressive components of borderline personality disorder—particularly impulsive aggression—prompted other studies of anticonvulsants. In addition to their anti-impulsivity and anti-aggressivity effects, anticonvulsants such as carbamazepine and phenytoin have demonstrated powerful mood-stabilizing effects. Researchers turned to divalproex specifically because it has been found useful in bipolar II disorder/cyclothymia and atypical depression, which have symptoms similar to those of borderline personality disorder. Divalproex has also been found to be useful in treating the hyperarousal/hyperreactivity of post-traumatic stress disorder and temper outbursts and aggressiveness, and anxiety, all symptoms of borderline personality disorder.

Eleven outpatients who met DSM-III-R criteria for borderline personality disorder on the Structured Clinical Interview for the Diagnosis of Axis II Disorders (SCID-II) were studied by Stein et al. in an 8-week, open-label trial of valproate supplied as divalproex. Patients had been in psychotherapy at least once a week for a minimum of 8 weeks prior to enrollment and continued psychotherapy for the duration of the trial. Medication was started at 250 mg/day p.o. and titrated, as tolerated, by up to 500 mg/day in order to reach blood divalproex levels of 50 to 100 µg/mL; no concurrent medications were allowed. Patients with current major depression, current or past psychotic disorder, current or past bipolar disorder, or major medical or neurologic disorder were excluded. A research psychiatrist rated the patients each week on the Hamilton Rating Scale for Depression (HAM-D), the Hamilton Rating Scale for Anxiety (HAM-A), and the OAS-M. A global scale developed by Cowdry and Gardner, similar to the CGI scale but assessing changes in mood, anxiety, anger, impulsivity, rejection sensitivity, and overall pathology, was also used to rate patient progress. Patients also completed the SCL-90.

The study was completed by 8 of the original 11 patients. Four (50%) of 8 completers were responders, rated “much less” or “less” by clinicians on change scores for overall pathology. Four (50%) of 8 patients were responders on scores for mood, and 3 (38%) were responders on change scores for anxiety, anger, impulsivity, and rejection sensitivity. Self-rated total SCL-90 scores decreased (improved) significantly (p = .03) from baseline to endpoint. HAM-D and HAM-A had decreased from baseline by the end of the trial, but the difference was not statistically significant. Likewise, the decrease on the total score for other-directed assault from baseline to endpoint on the OAS-M was not significant. Global subjective irritability on the OAS-M, however, decreased significantly (p = .02) from baseline to endpoint.

Stein and colleagues noted that patients’ HAM-D and HAM-A scores were not high at baseline and had not fallen significantly at endpoint, suggesting that improvements observed in mood and anxiety were better characterized as mood stabilization than as mood elevation. They suggested that, even though divalproex shows a broad spectrum of effects in borderline personality patients, the drug has specific effects on particular pathologic processes responsible for a spectrum of borderline personality disorder symptoms. They also cited evidence that mood instability and impulsivity are underlying biopsychological dimensions that characterize borderline personality disorder patients. If this relationship is correctly understood, interventions that change these dimensions will affect reversal of a variety of borderline personality disorder symptoms. The authors called for more extensive trials to
augment this small, open-label study. They urge that better prediction of treatment response be a goal of such future studies.

Hollander et al.35 recently completed a double-blind, placebo-controlled trial of divalproex in 21 patients with borderline personality disorder. An interim analysis of the first 16 patients—7 men and 9 women with a mean age of 34.8 years—was conducted. Patients with current major depression, current or past psychotic disorder, current or past bipolar disorder, or major medical illness were excluded. The authors35 examined whether divalproex therapy resulted in improvement in patients’ overall level of functioning as measured by both clinician and patient. The investigators were particularly interested in the effects of divalproex therapy in patients’ aggressive behaviors and affective instability. After a clinical assessment that included a psychiatric evaluation, patients were randomly assigned to receive either divalproex or placebo. Patient doses of divalproex started at 250 mg/day for 3 days and were titrated upward to 500 mg/day for 4 days. If divalproex was well tolerated, it was next administered to patients at 750 mg/day, and the dosage was then adjusted until blood divalproex levels of 80 µg/mL were reached. Global severity of patient illness was measured with the CGI-I scale, and the GAS was used to identify the lowest level of patient functioning over the preceding week. Additional outcome measures included the Aggression Questionnaire (AQ), which consists of 29 questions forming 4 subscales (physical aggression, verbal aggression, anger, and hostility); the Beck Depression Inventory (BDI), a 21-item self-report scale; and the OAS-M, which assesses behavioral irritability using 4 levels of severity in the categories of verbal aggression and physical aggression against objects, self, and others. Clinicians used the CGI, GAS, AQ, and BDI to assess patients at weeks 1, 2, 3, 4, 6, 8, and 10. In addition, an independent evaluator, a psychologist who was not monitoring any of the side effects associated with the medication, used the CGI, GAS, and OAS-M to evaluate patients at weeks 1, 6, and 10.

In this intent-to-treat analysis,35 patients randomly assigned to placebo were assessed CGI-I scores of 4—unchanged—at baseline. The same patients were minimally worse—with CGI-I scores of 5—at endpoint. Patients randomly assigned to receive divalproex were also rated 4 on the CGI-I scale at baseline, but at endpoint their CGI-I scores were 2—much improved—as assessed by both the clinician rater and the independent evaluator. Patients randomly assigned to placebo were assessed GAS-Global Severity scores of 53 at baseline and 50 at endpoint, while patients receiving divalproex scored 49 at baseline and 68—a substantial improvement—at endpoint. The higher GAS level shows a greater overall level of functioning. Again, improvement was assessed by both the clinician rater and the independent evaluator. Patients whose scores on the CGI-I scale were assessed as 1—very much improved—or 2—much improved—were considered responders. On that basis, none of the patients assigned to placebo—in the intent-to-treat group or in the complete group—were responders. In contrast, 60% of patients assigned to divalproex were responders in the intent-to-treat group, and 100% of those patients who completed the study were responders. The AQ and the OAS-M are 2 key measures of aggression. Patients taking placebo were rated 81 by the treating clinician at baseline and 98 (worse) at endpoint on the AQ. Patients taking divalproex were rated 79 by the treating clinician at baseline and 66 at endpoint. However, neither patients taking divalproex nor those taking placebo registered a change on any of the OAS-M measures, which led the researchers to question the scale’s sensitivity. Patients assigned to placebo registered scores of 14 at baseline on the BDI; patients taking divalproex were rated at 15.5. At endpoint, scores of 21 (worse) were registered by the patients taking placebo, while the scores of patients taking divalproex had improved to 2.6.

**CONCLUSION**

Aggression exists in both compulsive and impulsive disorders. SSRIs have specific effects in OCD.36 Anticonvulsants like divalproex and carbamazepine may prove useful in treating OCD patients with comorbid seizure disorders3 and neurologic soft signs.11 Studies also suggest a role for anticonvulsants such as divalproex, SSRIs such as fluoxetine and sertraline, and MAOIs such as tranylcypromine and phelinediazine in treating aggression and affective instability in borderline personality disorder. In both cases, more controlled trials with larger patient populations are necessary to replicate the results of existing research.

**Drug names:** alprazolam (Xanax), buspironine (BuSpar), carbamazepine (Tegretol and others), divalproex (Depakote), fluoxetine (Prozac), haloperidol (Haldol and others), phenelzine (Nardil), phenytoin (Dilantin and others), sertraline (Zoloft), thiocyanate (Navane), tranylcypromine (Parnate), trifluoperazine (Stelazine).

**REFERENCES**

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DISCLOSURE OF OFF-LABEL USAGE

The author of this article has determined that, to the best of his knowledge, the following agents mentioned in this article are not indicated for treatment of borderline personality disorder: anticonvulsants, antipsychotics, phenelzine, and SSRIs.