

Violent behavior: Choosing antipsychotics and other agents

Therapeutic options depend on whether patient violence is transient or persistent

When a patient with major psychiatric illness exhibits violent behavior, consider the course of violence in relation to his or her fixed and changing symptoms and deficits.^{1,2} Although most patients with schizophrenia, major depression, or bipolar disorder are not violent, effectively treating those who are calls for:

- differentiating between transient and persistent violent behavior
- providing medications and nonpharmacologic interventions shown to reduce each behavior
- addressing substance abuse and violent behavior concurrently.

Is violence transient or persistent?

Violent behavior is a common reason for psychiatric admission and prolonged hospital stays³ and a barrier to appropriate community placement⁴ and successful community reintegration.

Transient violence is limited to an acute psychotic episode; as psychotic symptoms abate, the violence resolves. Delusions, hallucinations, and conceptual disorganization are key triggers of transient violence.⁵ Excitement, anger, and agitation are its prominent symptoms.⁶

Treat a patient experiencing an acute violent episode with an oral first- or second-generation antipsy-



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Clinical Point
Emotional turmoil is usually less pronounced in patients whose violence is persistent

Table 1

Medications used to treat violence on an emergency basis

Drug	Route of administration*	Recommended dosage†
Benzodiazepines		
Lorazepam	IM or PO	1 to 2 mg IM or PO
Midazolam	IM	5 mg
First-generation antipsychotic‡		
Haloperidol	IM or PO	2 to 7.5 mg IM or PO
Second-generation antipsychotics‡		
Olanzapine	IM or PO	10 mg IM or PO
Risperidone	PO	2 to 6 mg
Ziprasidone	IM	10 to 20 mg

* Use oral medication if patient is cooperative; otherwise use an intramuscular injection.

† Lower dosages are used for elderly patients or those with dementia.

‡ Antipsychotics are not recommended for aggressive patients without a psychotic disorder or bipolar mania diagnosis.

chotic. For acute agitation, intramuscular (IM) delivery provides more rapid symptom resolution (*Table 1*). IM ziprasidone is approved for agitation associated with schizophrenia and IM olanzapine for use in agitation associated with schizophrenia or bipolar mania. Try talking calmly to the patient and explaining the need for medication (*Figure 1, page 66*). If this is not possible, a show of force might induce the patient's cooperation.⁷

For sedation, antipsychotic medication can be supplemented by lorazepam, the only benzodiazepine that is reliably absorbed when administered IM. Lorazepam has a relatively short half-life, and the usual dosage of 1 to 2 mg can be administered orally, sublingually, intramuscularly, or intravenously every 1 to 6 hours. Exercise caution, however, when respiratory depression is a possibility.

Persistent violence. Emotional turmoil is usually less pronounced in patients whose violence is persistent.⁸ Neurocognitive impairments, antisocial traits, and specific psychotic symptoms may exist singly or in combination in patients prone to persistent violence.

When a patient continues to be violent, consider poor treatment adherence or substance abuse, especially with outpatients (*Figure 2, page 68*).

Neurological and neurocognitive impairments are associated with persistent violence. Fairly broad impairments in various domains are seen on a variety of tests. Patients with neurocognitive impairment often present with impulsivity⁹ and deficits in behavioral adaptability.

In general, the consequences of a behavior determine its course; assaultive behavior usually decreases rapidly when strongly discouraged. Violent behavior that persists, therefore, suggests that neurocognitive impairment is causing a failure in behavioral adaptability.

Psychopathy, antisocial traits, and antisocial personality disorder (APD) also can result in persistent violence.

Antisocial personality is defined primarily by behavioral symptoms such as irresponsibility and criminal activities. Psychopathy also includes these symptoms but adds interpersonal and affective impairments such as callousness, grandiosity, and lack of remorse.

Psychopathy was the strongest clinical predictor of violence in a large trial of outpatients with major psychiatric disorders.¹⁰ APD, on the other hand, was the most significant clinical predictor of violent recidivism among offenders with mental illness in a meta-analysis of predictive longitudinal studies from 1959-1995.¹¹ In another study, psychopaths were about 5 times

Table 2**Medications used to treat persistent violence**

Drug	Initial dosage	Target dosage
Second-generation antipsychotics		
Clozapine	12.5 to 50 mg/d	300 to 450 mg/d*
Olanzapine	5 to 10 mg/d	15 to 30 mg/d
Quetiapine	50 to 100 mg/d	400 to 700 mg/d
Risperidone	1 to 3 mg/d	4 to 6 mg/d
First-generation antipsychotic		
Haloperidol	5 to 10 mg/d	10 to 20 mg/d
Mood stabilizers		
Carbamazepine	200 to 400 mg/d	1,000 to 1,400 mg/d*
Lithium	300 mg bid	300 mg tid*
Valproate	500 to 1,000 mg/d	1,000 to 1,500 mg/d*
Beta blockers†		
Nadolol	40 mg/d	80 to 140 mg/d
Propranolol	20 mg tid	200 mg to 600 (delayed onset of action)

* Serum levels should be obtained.
† Contraindicated for patients with cardiovascular disease, asthma, or diabetes.

more likely than nonpsychopaths to engage in violent recidivism.¹²

In addition to recidivism, the violence associated with psychopathy is characterized by its severity. Violence in these patients is often premeditated, deliberate, and goal-driven.

Persistent psychotic symptoms also play an important role in persistent violence and may represent treatment resistance. Some specific delusions, for example, are more likely to lead to violence and may persist despite overall improvement in psychotic symptoms.

Link et al¹³ have proposed that violence is more likely when a person has “threat/control override” delusions—if he believes people are seeking to

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*Data from a study comparing driving in 105 young adults with ADHD to 64 community control adults without the disorder.

Reference: 1. Barkley RA, Murphy KR, DuPaul GJ, Bush T. Driving in young adults with attention deficit hyperactivity disorder: knowledge, performance, adverse outcomes, and the role of executive functioning. *J Int Neuropsychol Soc.* 2002;8:655-672.

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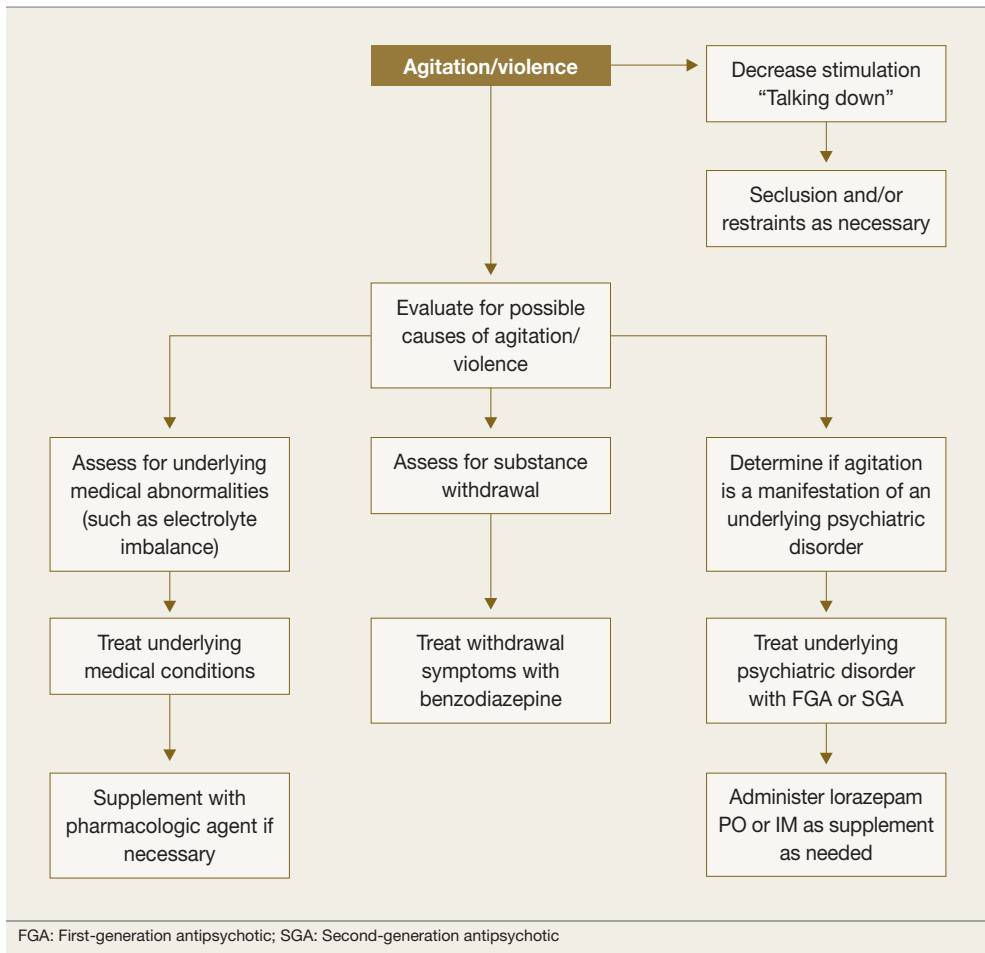
Violent behavior

Clinical Point

Delusions associated with violence are often chronic and well-circumscribed

Figure 1

Managing patients who present with acute violence or agitation



harm him or outside forces are controlling his mind.

Junginger stressed that violent themes in a patient's delusions are important predictors of violence.¹⁴ Delusions associated with violence are often chronic and well-circumscribed.

The role of antipsychotics

Pharmacologic intervention for violent behavior targets the underlying disorder, such as schizophrenia or bipolar disorder. Usual regimens used to treat patients with these disorders may need to be modified, however, for persistently violent patients (Table 2, page 65).

Second-generation antipsychotics (SGAs)—particularly clozapine—have superior antiaggressive properties beyond their antipsychotic or sedative effects, compared

with first-generation antipsychotics. Retrospective studies have shown clozapine can significantly decrease the number of violent incidents and episodes of seclusion and restraint.^{15,16} Evidence for efficacy of other SGAs in reducing physical assaults is more limited:

- Risperidone had a greater effect than haloperidol on hostility in a large, multi-center comparison trial.¹⁷
- Clozapine was more effective than haloperidol or risperidone in reducing hostility in a double-blind study of schizophrenia patients.¹⁸ This finding was independent of clozapine's antipsychotic effect.

Clozapine also was more effective than haloperidol in reducing the number and severity of aggressive incidents.¹⁹ The patients in this study, however, were not selected on the basis of aggressive behavior.

One large federally funded, double-blind, randomized trial compared clozapine, olanzapine, and haloperidol in 110 assaultive patients with schizophrenia or schizoaffective disorder. Patients had documented episodes of recent physical assaults and persistent aggressive behaviors during a 2-week period. Clozapine showed greater efficacy than olanzapine—and olanzapine greater efficacy than haloperidol—in reducing aggressive behavior.²⁰ This effect was independent of the drugs' antipsychotic and sedative actions.

Dual-diagnosis patients. Clozapine may be beneficial for patients with concurrent substance abuse because in addition to reducing aggression, it also may prevent relapse to substance abuse. In addition to intoxication, drug and alcohol abuse has disruptive effects on prefrontal function. These impairments play an important role in substance use-related aggression.

Substance abuse also can exacerbate psychotic symptoms, both directly and indirectly through poor treatment compliance. Patients with psychopathy are much more likely to abuse drugs. The association between drug abuse and violence can then be due in part to the higher percentage of psychopaths in the group of drug abusers.

Fortunately, patients with dual diagnosis who receive extensive substance abuse treatment show greater clinical improvement and better outcomes.²¹ Several studies found that clozapine was associated with decreased substance use. In one trial, schizophrenic patients with a history of drug abuse who received clozapine were much less likely to use substances over the next year than patients taking other antipsychotic medications.²²

Thus, clozapine has clear antiaggressive effects, but its use as a first-choice treatment for aggression is limited by the risk of side effects, in particular agranulocytosis. With careful blood monitoring, this complication is very rare, but persistently violent patients might not cooperate fully with the required monitoring.

Other medications

Other agents used to treat violent patients with mental disorders include mood stabilizers, beta blockers, and antidepressants.²³

continued



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Reference: I. Alpert J, Maddocks A, Nierenberg A, et al. Attention deficit hyperactivity disorder in childhood among adults with major depression. *Psychiatry Res.* 1996;62:213-219.

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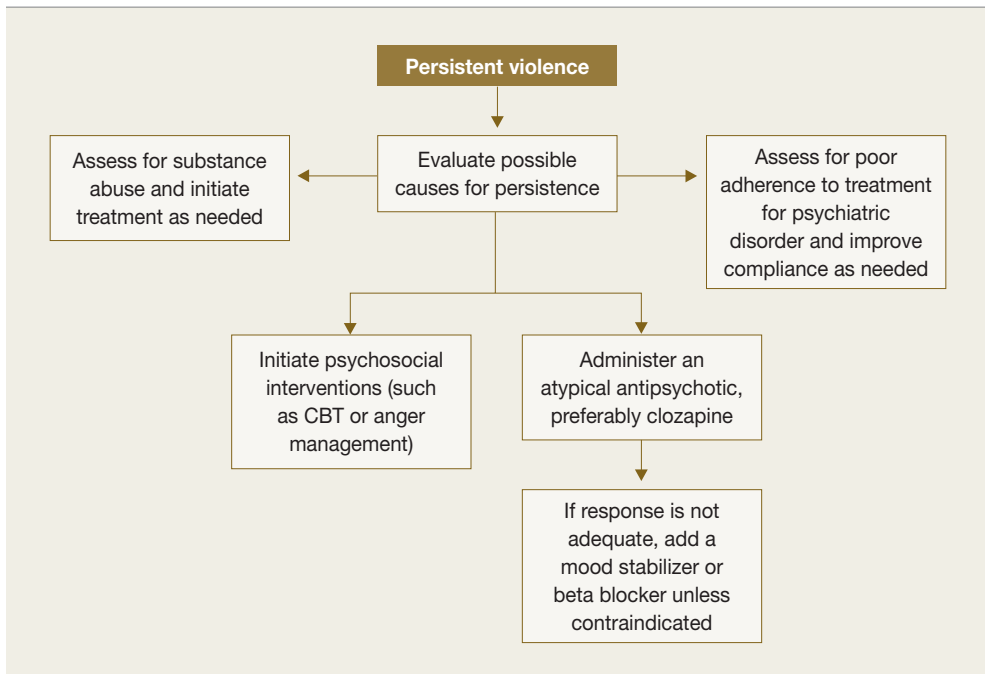
Violent behavior

Clinical Point

Patients whose behavior is violent might respond to a high degree of structure and supervision

Figure 2

Managing patients who exhibit persistent violent behavior



Mood stabilizers such as lithium, carbamazepine, or valproate might be useful as adjuncts to antipsychotic medications in managing assaultive patients with schizophrenia or other major psychiatric disorders. These medications might decrease violence by enhancing serotonergic activity.

Most evidence for mood stabilizers' anti-aggressive effect comes from studies of patients with personality disorders. Divalproex, for example, was more effective than placebo in reducing impulsive aggression in patients with Cluster B personality disorders.²⁴

Lithium reduces aggression and irritability in bipolar mania, while stabilizing the underlying disorder. Lithium can decrease aggression in other populations as well, including:

- the developmentally disabled
- prisoners with no apparent psychiatric diagnoses
- aggressive children and adolescents with conduct disorder
- adults with borderline personality disorder.

Beta blockers such as nadolol, pindolol, and propranolol have been reported to reduce aggression. Their usefulness is

limited, however, because they are contraindicated in patients with cardiovascular disease, asthma, or diabetes.

Antidepressants. Selective serotonin reuptake inhibitors may reduce impulsive aggression in nondepressed patients with personality disorders.²⁵

Nonpharmacologic treatments

To provide proper treatment, the clinician must understand the patient as a whole person, including his perception of his aggressive behavior. Nonpharmacologic interventions should be implemented with this in mind.

Compared with standard care, for example, intensive case management reduces the incidence of violence.²⁶

Behavioral techniques can decrease violence by addressing specific impairments underlying the violence. For example, improving a patient's cognitive functioning can counter impaired processing of feedback that is associated with neurological dysfunction.

Specific interventions, such as cueing to exaggerate the link between stimulus and response, could be beneficial.²⁷ Similarly,

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Bottom Line

When treating violent psychiatric patients, individualize medication and psychosocial components. In persistently violent patients, atypical antipsychotics—particularly clozapine—may reduce aggression, improve neurocognitive impairments associated with violence, and decrease substance use.

Related Resources

- Citrome L, Volavka J. Aggression. www.emedicine.com/med/topic3005.htm.
- Davidson RJ, Putnam KM, Larson CL. Dysfunction in the neural circuitry of emotion regulation—a possible prelude to violence. *Science* 2000;289:591-94.

Drug Brand Names

Carbamazepine • Carbatrol,	Olanzapine • Zyprexa
Equetro, Tegretol	Pindolol • Viskin
Clozapine • Clozaril	Propranolol • Inderal,
Divalproex • Depakote	Inderide
Haloperidol • Haldol	Quetiapine • Seroquel
Lithium • Eskalith, Lithobid	Risperidone • Risperdal
Lorazepam • Ativan	Valproate • Depacon
Midazolam • Versed	Ziprasidone • Geodon
Nadolol • Corgard	

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these patients might respond to a high degree of structure, supervision, and specific environmental modifications, such as transfer to a unit that specializes in treating violent patients.²⁸

In cognitive-behavioral therapy, patients can learn ways they can satisfy their needs without being violent. They also can be trained in problem-solving skills and in understanding the consequences of their actions. Such therapy might be useful for diminishing antisocial traits. Interventions aimed at preventing, decreasing, or counteracting arousal are important in addressing acute violence.

Anger management programs can help patients respond to interpersonal provocations in a more adaptive way.²⁹ These programs include:

- education about aggression
- self-monitoring of anger frequency, intensity, and situational triggers
- relaxation to reduce arousal and enable guided imagery training
- training in behavioral coping, communication, and assertiveness through role play
- practicing new anger-coping skills.³⁰

Tailor treatments to the dominant mechanisms underlying persistent violence.

References

1. Krakowski M, Czobor P. Violence in psychiatric patients: the role of psychosis, frontal lobe impairment and ward turmoil. *Compr Psychiatry* 1997;38:230-36.
2. Krakowski M, Convit A, Jaeger J, et al. Neurological impairment in violent schizophrenic inpatients. *Am J Psychiatry* 1989;146:849-53.

3. Lelliott P, Wing J, Clifford P. A national audit of new longstay psychiatric patients. I. Method and description of the cohort. *Br J Psychiatry* 1994;165:1609.
4. Bigelow DA, Cutler DL, Moore LJ, et al. Characteristics of state hospital patients who are hard to place. *Hosp Community Psychiatry* 1988;39:1815.
5. McNeil DE, Binder RL. The relationship between acute psychiatric symptoms, diagnosis, and short-term risk of violence. *Hosp Community Psychiatry* 1994;45:133-7.
6. Craig TJ. An epidemiologic study of problems associated with violence among psychiatric inpatients. *Am J Psychiatry* 1982;139:1262-6.
7. Allen MH. Managing the agitated psychiatric patient: a reappraisal of the evidence. *J Clin Psychiatry* 2000;61(suppl 4):11-20.
8. Krakowski M, Czobor P, Chou J. Course of violence in patients with schizophrenia: relationship to clinical symptoms. *Schizophr Bull* 1999;25:505-17.
9. Stein DJ, Hollander E, Cohen L, et al. Neuropsychiatric impairment in impulsive personality disorders. *Psychiatry Res* 1993;48:257-66.
10. Skeem JL, Mulvey EP. Psychopathy and community violence among civil psychiatric patients: results from the MacArthur Violence Risk Assessment Study. *J Consult Clin Psychol* 2001;69:358-74.
11. Bonta J, Hanson K, Law M. The prediction of criminal and violent recidivism among mentally disordered offenders: a meta-analysis. *Psychol Bull* 1998;123(2):123-42.
12. Serin RC, Amos NL. The role of psychopathy in the assessment of dangerousness. *Int J Law Psychiatry* 1995;18(2):231-8.
13. Link BG, Andrews H, Cullen FT. The violent and illegal behavior of mental patients reconsidered. *Am Sociol Rev* 1992;57(3):275-92.
14. Junginger J. Command hallucinations and the prediction of dangerousness. *Psychiatr Serv* 1995;46(9):911-14.
15. Wilson WH. Clinical review of clozapine treatment in a state hospital. *Hosp Community Psychiatry* 1992;43:700-3.
16. Volavka J, Zito JM, Vitrai J, Czobor P. Clozapine effects on hostility and aggression in schizophrenia. *J Clin Psychopharmacol* 1993;13:287-9.
17. Czobor P, Volavka J, Meibach RC. Effect of risperidone on hostility in schizophrenia. *J Clin Psychopharmacol* 1995;15:243-9.
18. Citrome L, Volavka J, Czobor P, et al. Effects of clozapine, olanzapine, risperidone, and haloperidol on hostility in treatment-resistant patients with schizophrenia and schizoaffective disorder. *Psychiatr Serv* 2001;52:1510-14.
19. Volavka J, Czobor P, Nolan K, et al. Overt aggression and psychotic symptoms in patients with schizophrenia treated with clozapine, olanzapine, risperidone, or haloperidol. *J Clin Psychopharmacol* 2004;24:225-8.
20. Krakowski M, Czobor P, Citrome L, et al. Atypical antipsychotic agents in the treatment of violent patients with schizophrenia and schizoaffective disorder. *Arch Gen Psychiatry* 2006;63:622-9.
21. Gonzalez G, Rosenheck RA. Outcomes and service use among homeless persons with serious mental illness and substance abuse. *Psychiatr Serv* 2002;53:437-46.
22. Brunette MF, Drake RE, Xie H, et al. Clozapine use and relapses of substance use disorder among patients with co-occurring schizophrenia and substance use disorders. *Schizophr Bull* 2006;32:637-43.
23. Citrome L, Volavka J. Psychopharmacology of violence, I: assessment and acute treatment. *Psychiatr Ann* 1997;27:691-5.
24. Hollander E, Tracy KA, Swann AC, et al. Divalproex in the treatment of impulsive aggression: efficacy in cluster B personality disorders. *Neuropsychopharmacology* 2003;28:1186-97.
25. Coccaro EF, Kavoussi RJ. Fluoxetine and impulsive aggressive behavior in personality-disordered subjects. *Arch Gen Psychiatry* 1997;54:1081-8.
26. Walsh E, Gilvarry C, Samele C, et al. Reducing violence in severe mental illness: randomised controlled trial of intensive case management compared with standard care. *BMJ* 2001;323:1093-6.
27. Becker ME, Vakil E. Behavioural psychotherapy of the frontal-lobe-injured patient in an outpatient setting. *Brain Inj* 1993;7:515-23.
28. Goldney R, Bowes J, Spence, N, et al. The psychiatric intensive care unit. *Br J Psychiatry* 1985;146:50-4.
29. Beck R, Fernandez E. Cognitive-behavioral therapy in the treatment of anger: a meta-analysis. *Cognit Ther Res* 1998;22:63-74.
30. Novaco, RW. *Anger control: the development and evaluation of an experimental treatment*. Lexington, MA: D. C. Heath, 1975.