

# The Medical Letter®

## On Drugs and Therapeutics

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### Drugs That May Cause Psychiatric Symptoms

Many drugs can cause psychiatric symptoms, but a causal connection is often difficult to establish. Psychiatric symptoms that emerge during drug treat-

ment could also be due to the underlying illness, previously unrecognized psychopathology, or psychosocial factors. The withdrawal of some drugs can cause symptoms such as anxiety, psychosis, delirium, agitation or depression.

**Table 1. Some Drug Classes**

Drug	Reactions	Comments
Amphetamine-like drugs	Bizarre behavior, hallucinations, paranoia, agitation, anxiety, mania, nightmares, insomnia	Usually with overdose or abuse; can occur with inhaler abuse; depression on withdrawal
Anabolic steroids	Psychosis, mania, depression, anxiety, aggressiveness, paranoia	Most reports based on abuse
Angiotension-converting enzyme (ACE) inhibitors	Mania, anxiety, hallucinations, depression, psychosis	Many reports
Anticholinergics	Confusion, memory loss, disorientation, depersonalization, delirium, auditory and visual hallucinations, fear, paranoia, agitation, anxiety	More frequent in elderly and children with high doses; can occur with transdermal scopolamine
	Sudden incoherent speech, delirium with high fever, flushed, dry skin, hallucinations, retrograde amnesia	From eye drops, particularly when mistaken for nose drops
Antidepressants, tricyclic	Mania or hypomania, delirium, hallucinations, paranoia, irritability, dysphoria, suicidality	Patients with bipolar disorder at highest risk for mania; anticholinergic effects may cause delirium in elderly; anxiety may occur with withdrawal
Antiepileptics	Agitation, confusion, delirium, euphoria, depression, psychosis, aggression, mania, toxic encephalopathy, nightmares, suicidality	Usually with high doses or high plasma concentrations; visual hallucinations with zonisamide <sup>1</sup>
Barbiturates	Excitement, hyperactivity, visual hallucinations, depression, delirium-tremens-like syndrome, disinhibition, parasomnias, anterograde amnesia	Especially in children and the elderly, or on withdrawal
Benzodiazepines	Rage, hostility, paranoia, hallucinations, delirium, depression, nightmares, parasomnias, anterograde amnesia, mania, disinhibition	During treatment or on withdrawal; may be more common in elderly
Beta-adrenergic blockers	Psychosis, delirium, anxiety, nightmares, hallucinations	With oral or ophthalmic preparations
Calcium-channel blockers	Depression, delirium, confusion, psychosis, mania	Several reports
Cephalosporins	Euphoria, delirium, delusions, depersonalization, illusions <sup>2</sup>	Renal disease is a risk factor
Corticosteroids (prednisone, cortisone, ACTH, others)	Psychosis, delirium, mania, depression	1%-3% incidence, may be dose-related; can also occur on withdrawal
Dopamine receptor agonists	Hallucinations, paranoia, delusions, confusion, mania, anxiety, depression, nightmares; impulse control disorders (pathological gambling, compulsive eating, hypersexuality) <sup>3,4</sup>	Many reports
Estrogens	Panic attacks, depression	Several reports
Fluoroquinolone antibiotics	Acute psychosis, confusion, agitation, depression, hallucinations, paranoia, Tourette-like syndrome, mania	Many reports
H <sub>1</sub> -antihistamines	Hallucinations, confusion, agitation, delirium <sup>5</sup>	With first-generation drugs. Rarely, if ever, with second generation
H <sub>2</sub> -antihistamines	Delirium, confusion, psychosis, mania, aggression, depression, nightmares	Especially in the elderly and seriously ill

**THE TABLES** — The following tables list some drug classes and some specific drugs reported to cause psychiatric symptoms. Such symptoms are reported uncommonly with most of the drugs listed. Alcohol, hallucinogens and other drugs not generally used for medical treatment in the US are not included. Withdrawal reactions in patients dependent on opioids and physiological reactions to drugs such as insulin have also been omitted. The table is limited to

psychiatric symptoms reported with single drugs, but drug interactions can also cause such symptoms (The Medical Letter Adverse Drug Interactions Program). Recent references and a few older ones are cited; additional older references are available in an earlier issue.<sup>1</sup> D

1. Drugs that may cause psychiatric symptoms. Med Lett Drugs Ther 2002; 44:59.

**Table 1. Some Drug Classes (continued)**

Drug	Reactions	Comments
Monoamine oxidase (MAO) inhibitors	Mania or hypomania, suicidality	
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Depression, paranoia, psychosis, confusion, anxiety	Probably more common with indomethacin <sup>6</sup> ; one case of exacerbation of psychosis in known schizophrenia with ibuprofen <sup>7</sup>
Opioids	Nightmares, anxiety, agitation, euphoria, dysphoria, depression, paranoia, psychosis, hallucinations, dementia	Usually with high doses; also occurs with intrathecal morphine, especially in elderly
Procaine derivatives (procainamide, procaine penicillin G)	Fear of imminent death, hallucinations, illusions, delusions, agitation, mania, depersonalization, psychosis	Probably due to procaine
Salicylates	Agitation, confusion, hallucinations, paranoia	Chronic intoxication
Selective serotonin reuptake inhibitors (SSRIs)	Mania, hypomania, hallucinations, suicidality	Anxiety, irritability, aggression or impulsivity on withdrawal
Sulfonamides	Confusion, disorientation, depression, euphoria, hallucinations	Several reports

**Table 2. Some Individual Drugs**

Drug	Reactions	Comments
Abacavir (Ziagen)	Depression, suicidal thoughts, auditory hallucinations, psychosis	Several reports <sup>8</sup>
Acetazolamide (Diamox*)	Depression, delirium, confusion, stupor	Especially in the elderly, or with renal disease, hypoalbuminemia or concurrent salicylates
Acitretin (Soriatane)	Depression, suicidal thoughts, aggressive behavior	Also reported with other retinoids; cause and effect not clear
Acyclovir (Zovirax*)	Hallucinations, fearfulness, confusion, insomnia, hyperacusis, paranoia, depression	At high doses, particularly in patients with chronic renal failure
Amantadine (Symmetrel*)	Illusions, visual hallucinations, delusions, depression, confusion; insomnia, anxiety, abnormal dreams, suicidality, aggression, paranoia, mania	Risk increases with duration of therapy; more common in elderly; abrupt discontinuation may cause psychotic symptoms
Atomoxetine (Strattera)	Irritability, temper tantrums, mania, suicidality <sup>9,10</sup>	
Azithromycin (Zithromax*)	Catatonia	One case report <sup>11</sup>
Asparaginase (Elspar)	Confusion, depression, paranoia	May occur frequently
Baclofen (Kemstro*)	Hallucinations, paranoia, nightmares, mania, depression, anxiety, confusion	Mainly after sudden withdrawal but also with therapeutic doses. <sup>12</sup> Can be life-threatening.
Bupropion (Wellbutrin*)	Psychosis, agitation, anxiety, nightmares, mania	Agitation, anxiety most common
Buspirone (BuSpar*)	Vivid dreams, delirium, mania, panic attack	In a few patients
Caffeine	Anxiety, confusion, psychotic symptoms	With excessive doses; anxiety on withdrawal
Chlorambucil (Leukeran)	Hallucinations, lethargy, seizures, stupor, coma	With high doses
Chloroquine (Aralen*)	Confusion, delusions, hallucinations, mania	Several reports <sup>13</sup>
Clarithromycin (Biaxin*)	Mania	Many reports
Clonidine (Catapres*)	Depression, delirium, psychosis, hallucinations	May resolve with continued use
Clozapine (Clozaril*)	Delirium	Less with slow dose titration; psychosis following abrupt withdrawal
Cyclobenzaprine (Flexeril*)	Hallucinations	Especially in elderly
Cycloserine (Seromycin)	Agitation, depression, psychosis, anxiety	Many reports
Cytarabine (Cytosar-U*)	Confusion	Especially with high doses
Dapsone	Insomnia, agitation, hallucinations, mania, depression	Several reports; may occur even with low doses
DEET (Off*)	Mania, hallucinations	With excessive or prolonged use
Desvenlafaxine (Pristiq)	Insomnia, mania, suicidality	Anxiety, irritability, abnormal dreams on withdrawal
Dextromethorphan (Robitussin*)	Psychosis	Several reports with high doses
Digoxin (Lanoxin*)	Delirium, depression, psychosis, mania, visual hallucinations	Dose-dependent; elderly at higher risk
Disopyramide (Norpace*)	Hallucinations, psychosis, paranoia, panic, depression	Within 24-48 hours after starting
Disulfiram (Antabuse)	Catatonia, delirium, depression, psychosis	Not related to alcohol reactions
Dronabinol (Marinol*)	Anxiety, psychosis, confusion	Most disturbing in the elderly
Duloxetine (Cymbalta)	Irritability, mania, nightmares, suicidality, exacerbation of PTSD <sup>14</sup>	Insomnia on withdrawal
Efavirenz (Sustiva)	Vivid dreams or nightmares, hallucinations, anxiety, depression, psychosis, confusion	Several reports

**Table 2. Some Individual Drugs (continued)**

<b>Drug</b>	<b>Reactions</b>	<b>Comments</b>
Erythropoietin (Epogen*)	Visual hallucinations	Reports in dialysis and bone marrow transplant patients
Eszopiclone (Lunesta)	Memory impairment, parasomnias, anterograde amnesia	
Gabapentin (Neurontin*)	Confusion, depression, suicidality	Anxiety and insomnia on withdrawal
Ganciclovir (Cytovene)	Psychosis, delirium, confusion	Several reports
Ifosfamide (Ifex*)	Encephalopathy, hallucinations, emotional lability, confusion, psychosis	Several reports, especially in elderly
Interleukin-2 (Proleukin)	Hallucinations, confusion	Especially with high doses
Interferon alfa (Roferon-A*)	Irritability, emotional lability, depression, agitation, paranoia, mania, suicidality	Contribution, if any, of concurrent ribavirin is unclear <sup>15</sup>
Isoniazid	Psychosis, hallucinations, mania	Several reports
Isotretinoin (Accutane*)	Depression, suicidality	Several reports
Ketamine (Ketalar*)	Nightmares, hallucinations, delirium, emotional lability	Acute; frequent with usual doses
Levodopa (Sinemet*)	Hallucinations, delusions, mania, depression, anxiety, panic attacks, confusion, nightmares	Dose-dependent; anxiety may occur in "off" phase
Lidocaine (Xylocaine*)	Hallucinations, psychosis, paranoia, delusions, agitation, anxiety	Several reports
Mefloquine (Lariam*)	Vivid dreams or nightmares, hallucinations, encephalopathy, depression, confusion, psychosis, aggression, agitation, anxiety	Vivid dreams and nightmares are frequent
Methyldopa	Depression, amnesia, nightmares, psychosis	Incidence of depression may be overestimated
Methylphenidate (Ritalin*)	Hallucinations, anxiety, encephalopathy	In children and adults
Metoclopramide (Reglan*)	Depression, anxiety, mania	Several reports; confusion in elderly
Metronidazole (Flagyl*)	Depression, agitation, emotional lability, confusion, hallucinations	Many reports
Modafinil (Provigil)	Euphoria, mania, delusions, hallucinations, suicidality	
Nevirapine (Viramune)	Hallucinations, delirium, psychosis, vivid dreams, depression	Several reports <sup>16</sup>
Ondansetron (Zofran*)	Panic attack, dysphoria	Occurs rarely
Oseltamivir (Tamiflu)	Delirium, delusions, hallucinations, nightmares, suicidality	Most reports (90%) are from Japan, and the majority were in children <sup>17</sup>
Pilocarpine (Salagen*)	Confusion, agitation, memory loss	Topical ocular use especially in elderly and demented patients
Pregabalin (Lyrica)	Euphoria, confusion, anxiety, disorientation, memory impairment, suicidality	
Propafenone (Rythmol*)	Agitation, delusions, disorientation, mania, paranoia	Several reports
Pseudoephedrine (Sudafed*)	Anxiety, hallucinations, paranoia, psychosis	Reported in children with usual doses
Quinidine	Confusion, agitation, psychosis	Usually dose-related
Ramelteon (Rozerem)	Abnormal thinking, agitation, mania, hallucinations, worsening of depression, suicidality	Several reports
Selegiline (Eldepryl*)	Hallucinations, mania, nightmares, behavioral disturbance, confusion, hypersexuality, delusions	Several reports
Sibutramine (Meridia)	Depression, psychosis, panic attacks	Several reports <sup>18</sup>
Sildenafil (Viagra)	Aggression, confusion, delusions, hallucinations, mania, paranoia	Several reports
Sodium oxybate (Xyrem)	Confusion, depression, disorientation, abnormal dreams, suicidality, psychosis, paranoia, agitation, hallucinations	
Thalidomide (Thalomid)	Reversible dementia	One report <sup>19</sup>
Theophylline	Mutism, hyperactivity, anxiety, mania	With high serum concentrations
Tizanidine (Zanaflex*)	Hallucinations	Reported in 3% of patients in clinical trials
Trazodone	Delirium, hallucinations, paranoia, mania	Several reports
Trimethoprim-sulfamethoxazole (Bactrim*)	Delirium, psychosis, depression, hallucinations	Several reports
Valganciclovir (Valcyte)	Depression, psychosis, hallucinations, confusion, agitation	
Varenicline (Chantix)	Agitation, depression, suicidality	Not clear whether these are caused by varenicline, nicotine or nicotine withdrawal <sup>20</sup>
Venlafaxine (Effexor*)	Visual hallucinations, insomnia, mania, suicidality	Few reports; anxiety, agitation, confusion, nightmares on withdrawal
Vinblastine	Depression, anxiety	May occur commonly and is dose-related
Vincristine	Hallucinations, depression	May be dose-related

**Table 2. Some Individual Drugs (continued)**

<b>Drug</b>	<b>Reactions</b>	<b>Comments</b>
Voriconazole (Vfend)	Hallucinations	One report of musical hallucinations <sup>21</sup>
Zaleplon (Sonata)	Illusions, anxiety, depression, hallucinations, parasomnias, anterograde amnesia	
Zolpidem (Ambien*)	Psychosis, hallucinations, sensory distortions, parasomnias, anterograde amnesia	Women may be at greater risk; higher doses may increase risk

\* Also available with other brand names or generically.

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