Features of tic disorders

Tic disorder
- Repetitive, purposeless, stereotyped movements (motor or vocal) that persist during sleep
- Intensity increased by excitement, anxiety or fatigue
- Sufferers attempt to disguise the movements by incorporating them into everyday activities
- Movements can be suppressed for minutes to hours, at the expense of increasing anxiety and compulsion to perform them

Mannerisms/habit disorders
- Tic disorder in 'normal' individuals

Transient tic disorder
- Motor or vocal tics lasting 4 weeks to 12 months

Chronic tic disorder
- Motor or vocal tics lasting › 12 months

Tourette's syndrome
- Motor and vocal tics
- Occur before the age of 18 years
- Last › 1 year
- Cause significant distress or functional impairment
- Other features may occur
  - Coprolalia (involuntary uttering of obscenities)
  - Copropraxia (involuntary obscene gestures)
  - Echolalia (repetition of others' speech)
  - Echopraxia (imitation of others' actions)
  - Pallilalia (repetition of the last word/phrase spoken)

2

Management: dopaminergic antagonists such as haloperidol and tetrabenazine are used to treat the chorea. Clonazepam may help sleep disorders. Counselling and antidepressants should be tried in those with mood disorders, and carbamazepine or valproate for behavioural problems. ◆

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Psychiatric effects of drugs for other disorders

C Heather Ashton

Neuropsychiatric effects account for up to 30% of adverse drug reactions (ADRs). Many of these ADRs, ranging from anxiety states to delirium, are caused by therapeutically administered non-psychiatric drugs, and many drugs can cause a variety of psychiatric effects. The incidence of such reactions is not always known because the information usually depends on selected patient groups or individual reports. In general, psychiatric ADRs are more common in elderly or ill patients and in those with a psychiatric history or family history. Other factors include metabolic status, drug interactions and personality. The ADRs are usually dose-related, but can occur at therapeutic doses and plasma concentrations in previously normal individuals with no innate vulnerability, and can also occur on drug withdrawal. The mechanisms are often complex and vary between drugs and clinical situations. Management may be simple if the cause is known, but patients who are taking several different drugs may need careful assessment.

A full discussion of all of the drugs that can cause psychiatric effects is beyond the scope of this contribution; a selection of the more common ADRs is given here.

Parkinson's disease and parkinsonism

Dopaminergic and antimuscarinic agents – dopaminergic drugs can cause depression, agitation, paranoid psychosis, mania, hypomania and excessive daytime sleepiness. The incidence of psychiatric problems was 20% in one series of 908 patients treated with levodopa for Parkinson's disease. Delirious states occurring with bromocriptine can be serious, involving confusion, aggressiveness, florid delusions and hallucinations, which can last for weeks after discontinuation of the drug. Similar effects have been reported with apomorphine, lysuride, pergolide and selegeline. These effects are usually dose-related but are exacerbated by antimuscarinic agents, which are often used concomitantly in Parkinson's disease and can also cause delirium. In addition, they can cause confusion and dementia, and may contribute to cognitive impairment in patients with Parkinson's disease.

Management of psychiatric symptoms in parkinsonism involves withdrawal or reduction of dose of the offending drug. The psychiatric effects of dopaminergic agents may be dose-limiting, particularly in elderly patients and those with post-encephalitic disease, and the appearance of symptoms may be delayed. Delirium caused by anticholinergic drugs or amantadine can be reversed rapidly with intravenous physostigmine. Benzodiazepine tranquil-

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Psychiatric effects of some drugs for other disorders

Disorders and drugs	Psychiatric effects
Parkinson's disease, parkinsonism	
• Dopaminergic agents (e.g. levodopa, bromocriptine, amantadine, apomorphine, lisuride, selegiline)	Delirium, depression, agitation, paranoid psychosis, mania, somnolence
• Antimuscarinic agents (benzatropine, biperiden, orphenadrine, procyclidine, benzhexol)	Exacerbate effects of dopaminergic agents; confusion and dementia
Chronic spastic conditions	
• Skeletal muscle relaxants (baclofen, dantrolene, tizanidine)	Anxiety, agitation, insomnia, nightmares, euphoria, confusion, hallucinations, withdrawal effects
Cardiovascular disorders	
• Digitalis preparations (digoxin, digitoxin)	Delirium, depression, hallucinations, psychosis
• Diuretics (causing potassium loss) (thiazides, frusemide, bumetadine, torasemide)	May exacerbate toxic effects of digitalis preparations
• β-adrenoceptor antagonists (e.g. propranolol, atenolol, metoprolol, oxprenolol, sotalol)	Sleep disturbance, nightmares, hypnogogic or hypnocampic hallucinations, depression, delirium
• Anti-arrhythmic agents (e.g. lignocaine, procainamide, mexiletine)	Psychotic reactions, depression
• Calcium channel blockers (e.g. nifedipine, diltiazem)	Psychotic reactions, depression
• Angiotensin-converting enzyme inhibitors (e.g. enalapril, imidapril, quinapril, ramipril)	Confusion, depression, nervousness, sleep disturbance
Endocrine disorders	
• Glucocorticoids (e.g. prednisolone, betamethasone, dexamethasone, triamcinolone)	Euphoria, mania, depression, psychosis, violent behaviour
• Oestrogens and progestogens (contraceptives, hormone replacement therapy, treatment of menstrual abnormalities)	Depression, premenstrual tension-like symptoms, changes in libido
• Male sex hormones and anabolic steroids (e.g. testosterone, nandrolone, stanozolol)	Depression, anxiety, changes in libido; mania, psychosis, aggression and withdrawal symptoms with high doses of anabolic steroids
Pain syndromes	
• Opioids (e.g. morphine, diamorphine, pethidine, dihydrocodeine, tramadol, pentazocine, nalbuphine, buprenorphine)	Dysphoria, depression, psychosis (particularly mixed agonists/antagonists), withdrawal symptoms
• Non-steroidal anti-inflammatory drugs (e.g. ibuprofen, diclofenac, pirioxicam, celecoxib, rofecoxib)	Nervousness, depression, drowsiness, insomnia; may aggravate depression and other psychiatric disorders
Gastrointestinal disorders	
• H_2-receptor antagonists and proton pump inhibitors	Depression, somnolence, insomnia
Bacterial, parasitic and viral infections	
• Antibiotics (e.g. chloramphenicol, streptomycin and related drugs, cephalosporins, isoniazid, cycloserine, quinolones)	Delirium, psychosis; sleep disorders, hallucinations, convulsions with quinolones
• Antimalarials (mefloquine, chloroquine, mepacrine, quinine)	Anxiety, panic, insomnia, nightmares, dysphoria, mania, psychosis, delirium
• Antivirals (aciclovir and related drugs, zidovudine and related drugs)	Drowsiness, hallucinations, depression, insomnia, anxiety
• Interferon-α, interferon-β	Depression and suicidal behaviour

lizers may be helpful, but antipsychotic drugs with antimuscarinic effects should be avoided.

Other medical conditions – bromocriptine has caused schizophreniform or manic reactions when used for post-partum suppression of lactation and in the treatment of pituitary tumours. Use of mydriatic eye drops containing antimuscarinics has been associated with delirium, hallucinations and amnesia.

Skeletal muscle relaxants such as baclofen used for chronic spastic conditions often cause sedation, and sometimes cause anxiety and agitation with insomnia. Other reported symptoms include euphoria, nightmares, confusion and hallucinations. The UK Committee on Safety of Medicines has warned that serious side-effects can occur on abrupt withdrawal of baclofen, which should be discontinued by gradual dose reduction over several weeks.

Cardiovascular disorders

Digitalis preparations can cause delirium, depression, hallucinations and psychosis. The effects are usually dose-dependent and the likelihood of psychiatric toxicity increases progressively with plasma digoxin concentration from 1.5–3 μg/litre. ADRs can also

occur at normal doses, particularly in combination with diuretics causing potassium loss. The mechanisms are probably multiple and include electrolyte disturbance and cerebral hypoxia resulting from cardiac failure. Management comprises discontinuation of the drug and correction of any hypokalaemia. Digoxin-specific antibody fragments are available for life-threatening toxicity.

β-adrenoceptor antagonists – the most common psychiatric effect of these drugs is sleep disturbance, including drowsiness, insomnia, vivid dreams, nightmares, and hypnogogic or hypnocampic hallucinations. These occur mostly with the lipophilic agents (e.g. propranolol), with which the incidence of drowsiness and fatigue is about 4%; vivid dreams and hallucinations at onset of sleep or waking are more common. The effects are generally dose-related, but have been reported in individuals taking propranolol at a dose of only 30 mg/day. Similar symptoms occasionally occur with water-soluble preparations such as atenolol. Both lipophilic and water-soluble agents can cause depression (incidence 1–5%) and both occasionally cause delirium.

Other cardiovascular drugs – psychotic reactions have been reported with several anti-arrhythmic agents and calcium channel blockers. Angiotensin-converting enzyme inhibitors may cause confusion, depression and nervousness.

Endocrine disorders

Glucocorticoids – long-term use of systemic glucocorticoids can cause a spectrum of psychiatric reactions in up to 5% of patients; these range from euphoria, mania and suicidal depression to schizophreniform paranoid psychosis with violent behaviour. Schizophrenia and epilepsy may be aggravated, and depressive reactions are more likely in patients with a positive family history. The effects are usually dose-related and can occur in patients with no psychiatric history. Long-term use leads to drug dependence, and psychiatric reactions of all types can occur on withdrawal. The therapeutic glucocorticoid dose varies widely between conditions and individual patients, but to minimize side-effects the maintenance dose should be kept as low as possible and withdrawal should be gradual.

Oestrogens and progestogens carry a slight risk of depression, particularly in women taking high-dose oestrogen. They may also cause a premenstrual-like syndrome with sodium and fluid retention, and can cause headaches and changes in libido.

Male sex hormones and anabolic steroids – testosterone can cause depression, anxiety, asthenia and changes in libido. Anabolic steroids can cause euphoria or depression, particularly at higher doses. They are sometimes abused in large doses by body-builders and athletes, and can lead to dependence. Psychiatric effects are common in this setting and may occur both during use and on withdrawal. In some studies, the incidence of mania and hypomania has been reported to be more than 20%, and psychosis and hallucinations more than 10%. Irritability, aggression and violence are also common. Depression, with risk of suicide, may be severe on withdrawal, and 50–80% of abusers report milder symptoms of fatigue, restlessness, insomnia, reduced libido and craving.

Pain syndromes

Opioids – pure opioid agonists such as morphine may cause dysphoria in 1–2% of patients treated for chronic pain, but the incidence of dysphoria, including depression, is much higher (10%) with mixed agonists/antagonists such as pentazocine and nalbuphine. Morphine and other opioids occasionally cause paranoid thinking and hallucinations, but psychotic reactions are more common with pentazocine and the non-opioid analgesic nefopam. Dependence is seldom a problem when the drugs are used clinically for pain relief. However, withdrawal reactions may occur, and discontinuation should be gradual and combined with other methods of pain control.

Non-steroidal anti-inflammatory drugs – all of these agents, including COX-2 inhibitors, can cause nervousness, depression, drowsiness or insomnia. The risk appears to be greatest with indomethacin, which may aggravate depression and other psychiatric disorders, epilepsy and Parkinson's disease.

Gastrointestinal disorders

Both H_2-receptor antagonists and proton pump inhibitors can cause depression, somnolence or insomnia, agitation and confusion with hallucinations, particularly in elderly or severely ill patients.

Bacterial, parasitic and viral infections

Antibiotics seldom cause psychiatric side-effects, but delirium and paranoid–hallucinatory psychosis have been reported with chloramphenicol, streptomycin and related drugs, cephalosporins and some antituberculous drugs. Quinolones can cause sleep disorders, restlessness, depression, confusion and hallucinations, and may induce convulsions in patients with or without a history of epilepsy.

Antimalarials – of these agents, mefloquine has the greatest propensity to cause neuropsychiatric effects. The incidence of severe reactions is only about 0.01%, but milder reactions are more common. The most common are anxiety, panic, insomnia, nightmares and dysphoria, which usually appear within 3 weeks of starting prophylactic dosing. Severe reactions include mania and paranoid–hallucinatory psychoses, which may also occur with chloroquine and mepacrine. Higher doses used for treatment of malaria may precipitate delirium. Mefloquine is contraindicated in patients with a history of neuropsychiatric disorder.

Antivirals – aciclovir and related drugs can cause drowsiness and hallucinations; protease inhibitors are associated with mood disorders including depression and sleep disturbances. Zidovudine and related drugs may cause general malaise.

Interferons – interferon-α and interferon-β may induce depression and suicidal behaviour. Interferon-β is contraindicated in patients with a history of severe depression or suicidal ideation. ◆

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