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PEER REVIEWED FEATURE
2 CPD POINTS

Sex, drugs and gambling

Disinhibition in older people

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It is important to understand the older person who presents with disinhibition of mood and behaviour. A careful consideration of possible causes, such as medications, dementia and bipolar disorder, is essential for appropriate management.

Key points

- **Disinhibition syndromes present with a spectrum of mood and behavioural changes that range from inappropriate behaviour in social situations to full-blown mania.**
- **Acute mania due to bipolar disorder with onset in early adult life is relatively uncommon in older people.**
- **In older people, a number of physical aetiologies, in particular medications, are more likely to precipitate disinhibition syndromes.**
- **Patients with frontotemporal dementia present with disinhibited behaviour early in the disease course, whereas such behaviours are commonly seen in patients in the later stages of Alzheimer's disease and vascular dementia.**
- **Lithium remains the treatment of choice in patients with bipolar disorder but its use must be managed carefully in this age group.**
- **In dementia, there is limited benefit from, and significant risks associated with, the use of antipsychotics.**

Although depression is the most common mood disorder presentation in older people, GPs may also be faced with patients displaying a variety of disinhibited behaviours, ranging from mildly inappropriate social behaviour to more severe changes in mood and behaviour that resembles hypomania or mania. The term 'disinhibition' is used here as an umbrella term because most older patients who present with such changes do not meet the full criteria for mania.[1]

Disinhibition syndromes that present for the first time in older people are far more likely to be due to an associated physical aetiology than be primary mania due to bipolar disorder. Secondary mania refers to presentations associated with neurological or systemic disease, in the absence of a history of mood disorder, to which older people are more vulnerable. Secondary mania should be considered when there is direct temporal association between the mood symptoms and the physical aetiology and when symptoms precede, or resolve upon cessation of, the physical comorbidity. The box shows some common causes of disinhibition in older people.

There are significant implications for treatment in distinguishing between primary and secondary mania, namely whether to consider the use of medium- or long-term mood-stabiliser medications.

PRIMARY MANIA

The prototypical cause of disinhibition is acute mania, which is a mood episode of at least one week duration marked primarily by:

- irritable or elevated affect
- acceleration of thinking

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CAUSES OF DISINHIBITION IN OLDER PEOPLE

Primary mania

- Bipolar I disorder

Secondary mania/disinhibition syndromes

- Medications
  - corticosteroids
  - dopamine agonists (e.g. for Parkinson's disease)
  - non-SSRI antidepressant classes: especially tricyclic antidepressants and venlafaxine
- Cognitive disorders
  - delirium
  - frontotemporal dementia (behavioural variant)
  - other dementias with associated executive dysfunction (e.g. Alzheimer's disease, vascular dementia)
  - traumatic brain injury
- Others
  - substance use disorders
  - tumours
  - infections

- increase in energy and physical drive.

There is little to distinguish mania from other causes of disinhibition with regard to clinical presentation and severity according to chronological age or age of onset. Although risks may not appear significant in the older person, these must be considered in context. For example, the 80-year-old man who insists on renovating his home single-handedly poses a risk of physical harm to himself from climbing ladders. Or if he insists on giving away seemingly small amounts of money he is jeopardising his finances.

Most presentations of mania in older people are due to a relapse of early-onset bipolar disorder, which most commonly has its onset in the 16 to 25 year age group. In addition, always consider the possibility of late-onset presentations; the incidence of bipolar disorder in men declines with age to the mid-50s, and then increases again such that new cases are as common in the over 75s as they are in men in their mid-30s.[2] These presentations may be associated with a positive family history of mood disorder.

SECONDARY MANIA

Older people who present with new-onset symptoms of mania typically have an underlying medical correlate. By far the most common causes are electroconvulsive therapy (ECT) and prescribed medications including:

- corticosteroids
- dopamine agonists used in patients with Parkinson's disease (i.e. bromocriptine, pramipexole, ropinirole and apomorphine)
- non-selective serotonin reuptake inhibitor (SSRI) antidepressant classes (especially tricyclic antidepressants and venlafaxine).

Up to 25% of patients prescribed oral corticosteroids may develop symptoms of mania, typically early in the course of treatment and for prednisone at doses of more than 40 mg/day.[3]

About 15% of people with Parkinson's disease experience an impulse control disorder, such as pathological gambling, compulsive shopping, compulsive sexual behaviour and binge eating.[4] In most cases, the behaviour improves after withdrawal of the dopaminergic agent.

This is well illustrated by the case of a premorbidly sober professional in his 70s with Parkinson's disease who was prescribed pramipexole and then began to frequent brothels for the first time in his life. He was even persuaded to invest in the business by the owner of the establishment. The effects of his behaviour on his family and finances were, needless to say, devastating.

Another syndrome seen in 3 to 14% of patients with Parkinson's disease is 'punding', which consists of complex and stereotyped behaviours that resemble the physical drive of mania.[5] Examples include cleaning, repairing, gardening, writing, artistic drawing, excessive computer or internet use, and repeatedly categorising objects or information. Punding is associated with the use of dopaminergic agonists and impulse control disorder, and typically occurs in males with a younger age of onset (under 50 years) of Parkinson's disease.

In another case of a man in his 70s with a history of recurrent insertion of foreign bodies per rectum and a fondness for viewing online pornography, it was not so clear if the prescription of pramipexole was causative. Further questioning revealed the man had a longstanding enjoyment of pornography and had exposed himself to young women before the onset of Parkinson's disease. The withdrawal of the drug was associated with a significant increase in motor symptoms and disability, and no significant change in behaviour. This case highlights the need to also assess the premorbid personality of the disinhibited individual.

Antidepressant-induced 'switching' from depression to mania is seen in about 8% of patients with unipolar depression and no history of hypomania or mania.[6] The risk is greater with the use of tricyclic antidepressants and other broad-spectrum agents such as venlafaxine, than with SSRI use, and may be increased further by an additional history of alcohol or substance use disorder and cerebrovascular disease. Although there is some uncertainty, patients with antidepressant-induced (and, for that matter, ECT-induced) mania are considered by many practitioners to lie on the bipolar spectrum.

Illicit substance use should also be considered, especially in the 'young old' who 'came of age' in the 1960s. Both stimulants, especially (methyl)amphetamine-like agents, and hallucinogens may be associated with secondary mania.

Other causes such as stroke or tumour are rare. Post-stroke mania typically follows a right cerebral infarct, with the common symptoms being elevated mood, increase in speech, insomnia and agitation.[7]

Delirium

Delirium is an acute confusional state most frequently due to infectious or metabolic causes or medication use. It mimics features of all the major psychiatric syndromes including mania.

Delirium is distinguished from mania primarily by the associated change in cognition towards a clouded sensorium, the tendency for symptoms to fluctuate and reversal of the sleep–wake cycle. This means that the person with delirium may sleep during the day and be awake at night, whereas the person with mania tends to be always 'on the go'. The distinction, however, can be difficult because cognitive symptoms may be a prominent part of mania in an older person.

Dementia

There are two main presentations of disinhibition in dementia. The more common is as a behavioural and psychological symptom of dementia (BPSD), a term that refers to the noncognitive symptoms of dementia, seen in about 60% of patients typically with moderate-to-severe dementia.[8] Such behaviours tend to occur at certain characteristic times of the day, in particular the 'sundowning' effect of the late afternoon and early evening. They tend to be transient, lasting weeks or months within a condition that lasts typically at least a decade.

In particular, agitated behaviours may be associated with examples of increased physical drive, often in the absence of obvious goals as is the case in mania, such as:

- opening and closing drawers
- restlessness – for example, pacing up and down in a particular area
- dressing and undressing repeatedly
- screaming or yelling.

Similarly, aggression can be either physical or verbal, and range in severity. Examples include:

- angry outbursts, often for no good reason
- swearing that is out of character for the person
- threatening other people
- pushing, hitting or grabbing.

In addition, sexual disinhibition such as a patient exposing themselves or making inappropriate physical contact with a carer may be seen.

The second presentation of disinhibition associated with dementia is more specific. This form of dementia was formerly known as Pick's disease but has been reclassified as frontotemporal dementia with either behavioural or language (i.e. semantic dementia or progressive non-fluent aphasia) variants.

About 15% of people with Parkinson's disease experience an impulse control disorder. In most cases, the behaviour improves after withdrawal of the dopaminergic agent.

Behavioural-variant frontotemporal dementia (bvFTD) is marked by atrophy of the frontal lobes and changes in personality and interpersonal conduct that occur early and typically without obvious changes in cognition such as short-term memory loss.[9] This contrasts with disinhibited behaviours in patients with Alzheimer's disease and vascular dementia, which occur much later in the course of the disease as a BPSD. FTD is the second most common cause of early-onset dementia occurring before the age of 65 years and may be misdiagnosed as mania.

Typical features of bvFTD, which may be misinterpreted as personality dysfunction, include:

- a loss of social grace and manners such as touching or kissing unfamiliar people
- making offensive jokes
- making sexually inappropriate remarks
- a change in eating pattern, including very messy or fast eating that may include the plate being licked
- pathological gambling.

It is important to note that the person with bvFTD will also present with features of apathy, which is not the case in mania, such as:

- a lack of motivation and drive to perform usual activities
- indifference to others' feelings
- loss of emotional warmth and reaction.

Huntington's disease and HIV-associated dementia may also present with disinhibition.

MANAGEMENT

Primary mania due to bipolar disorder

The treatment of choice for both patients with acute mania and those in the maintenance phase of bipolar disorder remains lithium. A serum level in the range of 0.5 to 0.8 mmol/L that balances efficacy and tolerability is appropriate.[10] Levels will need to be slightly higher in patients with acute mania.

The key factors for managing lithium use in the older person are to:

- ensure the serum lithium level is measured exactly 12 hours post-dose, because interpretation of the results is not possible otherwise
- avoid or minimise the use of concurrent medications that can increase the serum level, such as diuretics/ACE inhibitors and NSAIDs/COX-2 inhibitors
- repeat measurement of the serum level on a regular basis, every three to six months or more frequently if there is comorbid renal impairment, diabetes insipidus, thyroid disease or concurrent use of the medications listed above
- ensure judicious reduction in the lithium dose in patients on long-term treatment given the age-related decline in glomerular filtration rate (GFR).

Many older, otherwise clinically stable patients will present with renal impairment or lithium toxicity, which should lead to re-evaluation of the dose, rather than

immediate substitution with another agent. Of the alternative mood stabilisers, there is less evidence of benefit for sodium valproate as a monotherapy in the maintenance phase of treatment and atypical antipsychotics such as olanzapine and quetiapine are associated with significant neurological and metabolic adverse effects. Abrupt cessation of lithium is associated with an increased risk of mania and should be avoided.

Patients with chronic renal disease may be maintained on lithium provided there is regular monitoring of renal function and consultation with a renal physician. For example, it has been recommended that patients with an estimated GFR (eGFR) in the range of 30 to 59 mL/min should receive review of urea, electrolytes and creatinine levels and eGFR, urinalysis and assertive treatment of cardiovascular risk factors every three months.[11]

Secondary mania

Patients with secondary mania require a thorough investigation of potential underlying causes, in conjunction with an appropriate specialist physician colleague and/or psychiatrist. Neuroimaging is essential to exclude the presence of tumours and determine the extent of cerebrovascular disease.

GPs should have an understanding of the psychological or behavioural adverse effects of the drugs commonly associated with disinhibition and, most importantly, warn the patient or carer of these potential problems.

Most cases of mania or disinhibition that are drug induced will resolve or improve with dose reduction or withdrawal. If symptoms are more severe or persistent, the short-term use of a low-dose antipsychotic such as risperidone 0.5 to 1 mg/day may be required.

Dementia

Psychotropic medications have limited benefits in treating patients with behaviours such as agitation and aggression, as well as having the potential to produce serious or life-threatening side effects.[8]

Despite these limitations, antipsychotics remain the most widely used medications to treat patients with disinhibition behaviours in dementia. In this patient group, antipsychotic medications have been associated with:

- an increased risk of stroke, especially in the presence of cardiovascular risk factors
- an increased risk of death
- neurological problems including Parkinsonism and akathisia, a form of motor restlessness
- worsening of cognition
- metabolic adverse effects (increase in blood glucose, lipids, weight)
- cardiac problems (raised QTc interval, which is associated with sudden death).

In a clinical emergency, the use of low-dose atypical antipsychotics, such as risperidone 0.25 to 1 mg/day, is preferred. Olanzapine and quetiapine may be associated with over-sedation and increased risk of confusion because of their anticholinergic activity. The typical antipsychotics such as haloperidol or thioridazine should be avoided, as should long-acting depot injections.

The benzodiazepine medications are also commonly prescribed for patients with dementia, mainly to ensure they get an adequate amount of sleep. Apart from the specific risk of tolerance, benzodiazepines are also associated with an increased risk of confusion and falls, as are the antipsychotics.

It is recommended that psychotropic medications, other than the antipsychotics and benzodiazepines, be considered initially for the treatment of patients with dementia. However, these have their own risks.

- The antidepressant citalopram 10 to

20 mg/day has comparable efficacy to antipsychotics for the treatment of patients with agitation and aggression (off-label use).
- The anticonvulsant carbamazepine 100 to 300 mg/day is used for the treatment of patients with agitation (off-label use).
- Analgesic medications, such as paracetamol or, if necessary, buprenorphine patches, are also helpful for the treatment of patients with agitation (off-label use), independent of any effect on pain.

Caution is recommended in the use of all psychotropic medications in patients with dementia. In particular, they should not be used in isolation – behavioural and psychosocial treatments should be tried first or at the same time. Behavioural treatments are best delivered by psychologists and allied health professionals who specialise in this area. GPs may refer patients to the nationwide Dementia Behaviour Management Advisory Service (24-hour helpline 1800 699 799).

Consent for the use of psychotropic medications should be obtained appropriately. This may be available from the patient or, if the patient lacks this specific capacity, a substitute decision maker, such as a legally defined 'person responsible' or your state's guardianship tribunal or equivalent. The legal requirements will vary from state to state.

The 3T approach to psychotropic use in patients with dementia is a useful model to remember.[8]
- **Target the symptoms to be treated.** Patients with aggression and psychosis may respond to medication; those who wander and call out will not.
- **Titrate ('start low, increase slow').** Doses should be one-quarter to one-half of those used in younger patients.
- **Time limited use.** Review drug use regularly, withdraw if ineffective or causing side effects, and avoid polypharmacy. As behaviours tend to be transient, consider withdrawal after 12 weeks even if effective – most behaviours will not deteriorate.

CONCLUSION

Disinhibition behaviours in older people may range from sexually indiscreet remarks or actions, pathological gambling and physical agitation to full-blown mania. However, it is important to go beyond consideration of bipolar disorder and to explore other possible causes such as medications, delirium and dementia. Management should be in conjunction with an appropriate medical specialist or a specialist dementia advisory service. Psychotropic drugs such as lithium and antipsychotics must be used with extra caution in this age group. MT

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