Delirium

Delirium is common and affects patients throughout the hospital under the care of many specialties (Ryan et al, 2013). It can cause significant psychological distress to patients, families and health-care providers (Partridge et al, 2013). As such, it is a problem that is frequently brought to the attention of junior doctors on the ward. This article explores the literature on delirium.

Delirium is defined as an acute decline in cognitive function (Inouye et al, 2014) and it occurs in hyperactive, hypoactive and mixed forms (Marcantonio, 2017). It can be thought of as an acute brain failure, analogous to acute heart failure (Inouye et al, 2014). Those with more predisposing factors need fewer precipitating factors to develop it. Two of the most important predisposing factors are increased age and preexisting cognitive impairment (van Velthuijsen et al, 2018) and thus older people often develop delirium secondary to minor precipitants such as urinary tract infection or constipation, with 35% of hospitalized patients aged 80 years or older having delirium (Ryan et al, 2013). However, it can also occur in any patient when exposed to a major stress, with up to 80% of patients on intensive care units having delirium (Ely et al, 2001).

Is delirium important?

The significance of a diagnosis of delirium is often underestimated because of its generally transient nature. However, a growing body of evidence suggests that cognitive decline is not a linear decline with age, but instead a step-wise decline associated with medical illnesses and delirious episodes (Mathews et al, 2014; Davis et al, 2017). Animal models have shown that systemic inflammatory insults accelerate and exacerbate permanent loss of neurological function (Cunningham et al, 2009), and in older people episodes of delirium are associated with an accelerated decline in mini-mental state examination (MMSE) score (Davis et al, 2017). A meta-analysis by Witlox et al (2010) showed that after an episode of delirium, older people were at significantly increased risk for future institutionalization, de novo dementia and death. Hospitalization itself may also have an effect (Mathews et al, 2014).

Dr Lloyd Steele, Core Medical Trainee, Department of Medicine, Queen Alexandra Hospital, Portsmouth Hospitals NHS Trust, Portsmouth PO6 3LY

Dr Georgios Aperis, Consultant Geriatrician, Department of Medicine, Queen Alexandra Hospital, Portsmouth Hospitals NHS Trust, Portsmouth

Correspondence to: Dr L Steele (Lloyd.steele@nhs.net)

Investigating delirium

There are a myriad of potential precipitants for delirium (Marcantonio, 2017) and multiple causes are often identified. A broad work-up is thus recommended, with history and examination the first steps (Inouye et al, 2014; Marcantonio, 2017; Oh et al, 2017). The history should include a collateral history to understand the patient's baseline and the timeline of decline (Oh et al, 2017). This helps to exclude mimics of delirium, such as depression and behavioural and psychological symptoms of dementia (*Table 1*). Dementia with Lewy bodies is an especially difficult mimic as fluctuations are a common feature – as well as perceptional disturbances and delusions – and although associated with a persistent decline in cognition over time, a systematic review by Cole et al (2009) showed that delirium can also be persistent (in 45% at discharge and in 21% at 6 months).

Investigations

Laboratory tests needed in patients with delirium depend on the clinical situation (Marcantonio, 2017). Screening for infection is important, but note should be made that although urinary tract infection is a common precipitant, asymptomatic bacteriuria is also common in older people – for which antibiotic treatment is not needed (Trautner and Grigoryan, 2014). Additional tests which are useful in select situations include cerebral imaging (in patients with head trauma or new focal neurological findings), lumbar puncture (if findings suggest meningitis or encephalitis), and electroencephalography (if seizures are suspected) (Marcantonio, 2017).

A 2003 survey suggested that delirium is over-investigated, with 18% of respondents selecting an unnecessary diagnostic test (cerebral imaging, lumbar puncture or electroencephalography) when the case provided did not suggest that it was needed (Carnes et al, 2003). Excessive investigation does not generally contribute to the diagnosis. For computed tomography head scans, one study showed a yield rate of 1.5% in the absence of new neurological findings, a reduction in consciousness or a recent fall (Lai and Wong Tin Niam, 2012). It also adds to financial costs, and may exacerbate confusion or agitation through

Table 1. Confusion Assessment Method (CAM) diagnostic criteria for delirium and the presence of these features in delirium and mimics of delirium

CAM criteria for delirium	Delirium	Dementia	Depression	Psychosis
Acute change in mental status with fluctuating course	+	-	-	±
Inattention	+	±	±	±
Altered level of consciousness	+	-	-	-
Disorganized thinking	+	±	-	+
Altered psychomotor activity	+	±	+	+

From Oh et al (2017)

the investigations themselves – especially if sedation is needed.

Criteria

Diagnostic criteria can be used to confirm the diagnosis of delirium, such as the confusion assessment method criteria or Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria (*Table 1*) (National Institute for Health and Care Excellence, 2010). However, specific issues with the confusion assessment method are that it requires a trained tester and an independent cognitive test (e.g. MMSE), and thus the National Institute for Health and Care Excellence also emphasized the need for research on a new screening tool. In recent years, 4AT has gained popularity nationally and internationally and has the advantage of containing a cognitive test and not requiring training (Shenkin et al, 2018).

Screening may help to detect more cases of delirium. One study showed that when a screening tool was used – either spatial span forwards or months backwards – approximately twice as many cases were detected compared to clinical documentation or nursing staff interview (Ryan et al, 2013). However, barriers to implementation include time, cost, and the absence of evidence that systematic case finding of delirium improves patient outcomes (Marcantonio, 2017). Potential advantages of screening include early identification and treatment of distress in elderly patients, allowing family members to be informed, and raising the awareness of the need for careful capacity assessment.

Managing delirium

The British Geriatrics Society (2016) emphasizes multifactorial management for delirium, including:

- Treating infection (when present)
- Assessing and treating any dehydration
- Addressing nutritional status
- Treating constipation
- Identifying and treating urinary retention, controlling pain
- Encouraging mobility
- Re-orientation strategies
- A medication review.

A medication review needs to address both the types and total number of medications as, although certain medications are of particularly high risk of causing or exacerbating delirium (*Table 2*), polypharmacy itself also contributes (Cerveira et al, 2017). Anticholinergic burden scales should be considered for all elderly patients. These aim to quantify the cumulative effect of medications with anticholinergic effects, which includes cognitive impairment (Pfistermeister et al, 2017).

Treating patients with delirium can be difficult, especially those with the hyperactive variant, who can be agitated, aggressive, refuse to cooperate, and have a disturbed sleep–wake cycle (van Velthuijsen et al, 2018). This can cause distress to the patient, as well as his/her relatives and health-care professionals, lead to suboptimal treatment of any precipitating factor, and risk harm, such as falls. Prioritizing safety for these patients is important, and such measures include one-to-one monitoring of high-risk patients, monitoring bays, the use of fall alarms for patients at high risk of falling, and asking family members to come in, who often elicit a more positive response from the patient. However, management can be time-intensive: nurses spend on average an extra 240 minutes, and physicians an extra 66 minutes, on the care of patients with delirium compared to controls (Weinrebe et al, 2016). This problem is compounded by the symptoms of delirium tending to occur or worsen during evenings and nights, the so-called 'sundowning syndrome', when staffing levels are often lowest. This can lead to a situation where the junior doctor covering the ward is asked to prescribe medications to try to reduce the hyperactivity. In this context one can feel that not prescribing medication is difficult, as if one is omitting a valid treatment and instead permitting the challenging situation to continue. But what is the evidence? Should we be prescribing these patients haloperidol or lorazepam, or are we wilfully ignoring the problem if we choose not to?

Medications

Antipsychotics such as haloperidol have been used for decades to treat delirium, but evidence for their use is conflicting. A meta-analysis by Neufeld et al (2016) reported that antipsychotics were not associated with a change in delirium severity, incidence nor duration, but another by Kishi et al (2016) reported that antipsychotics were superior to placebo in terms of improving delirium severity rating scores. The decision to use an antipsychotic must involve a trade-off between the potential benefits, especially in patients with delusion and hallucinations, against the potential risks (Marcantonio, 2017).

Table 2. High risk medications for delirium and potential alternatives

Drug	Mechanism of adverse effect	Alternatives
Benzodiazepines	CNS sedation, withdrawal	Non-pharmacological sleep protocol
Barbiturates	CNS sedation, withdrawal	Gradual discontinuation or benzodiazepine substitution
Non-benzodiazepine sedative hypnotics (e.g. zolpidem)	CNS sedation, withdrawal	Non-pharmacological sleep protocol
Opioids, especially meperidine	CNS sedation Anticholinergic Faecal impaction	Paracetamol Try use on an 'as required' basis rather than regularly Topical non-steroidal anti-inflammatory drugs
Antihistamines	Anticholinergic +/- CNS sedation	Non-sedating antihistamines
Anticholinergics (e.g. oxybutynin)	Anticholinergic	Lower dose Non-pharmacological measures (if not already tried), e.g. weight loss if appropriate, bladder training Mirabegron
Tricyclic antidepressants	Anticholinergic	Selective serotonin-reuptake inhibitors Serotonin-noradrenaline reuptake inhibitors

By the American Geriatrics Society Beers 2015 Criteria Update Expert Panel (2015), Marcantonio (2017)

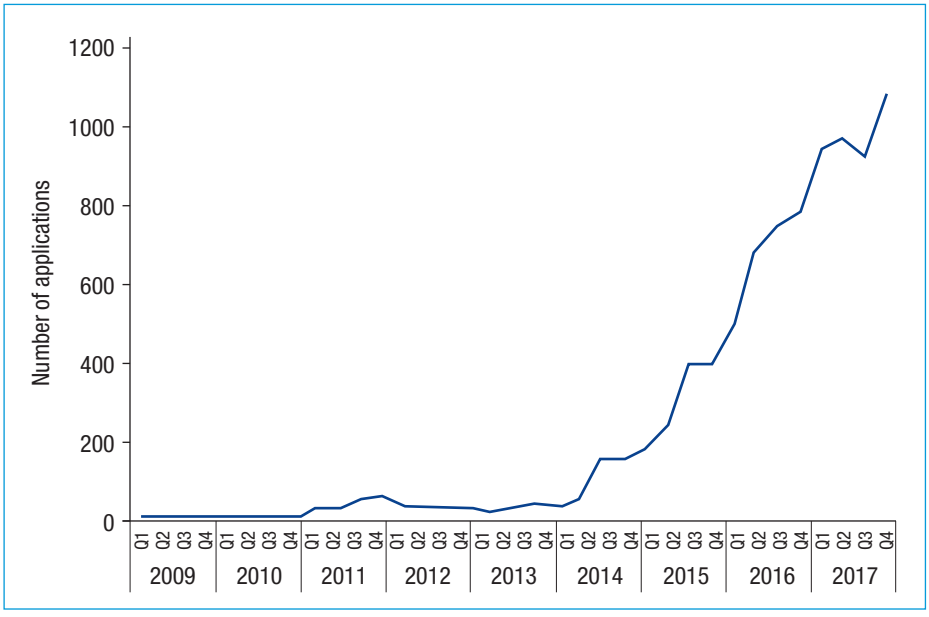

Figure 1. Deprivation of liberty safeguards applications from January 2008 to September 2017. From Ministry of Justice (2017).

The adverse effects include extrapyramidal symptoms, neuroleptic malignant syndrome, QT interval prolongation, predisposing to arrhythmias, and anticholinergic effects. The natural aging process, including increased blood–brain barrier permeability, predisposes older people to these side effects, and specific concerns in older people are of increased cerebrovascular events and increased all-cause mortality (Thom et al, 2017).

The National Institute for Health and Care Excellence (2010) guideline for delirium – which is similar to consensus statements from other organizations, including the American Geriatrics Society and the Canadian Coalition for Seniors' Mental Health – therefore only advocates antipsychotic use when a patient is in distress and poses a safety risk to him-/herself or others, after verbal and non-verbal de-escalation techniques have already been tried. It suggests that either haloperidol, a typical antipsychotic, or olanzapine, an atypical antipsychotic, can be used. Prospective studies have suggested that atypical antipsychotics may be better because they have a faster onset of action and lower incidence of extrapyramidal symptoms, despite a potentially greater risk of orthostatic hypotension (Thom et al, 2017). The initial dose should be low, such as haloperidol 0.5 mg or olanzapine 2.5 mg, and additional doses added if needed as there is a wide variability in response between patients (Marcantonio, 2017). The authors recommend only prescribing stat doses or a 2–3-day course as any prescriptions made on an as required basis may end up being given frequently over a prolonged period, and National Institute for Health and Care Excellence (2010) recommends that antipsychotics should be used for less than 1 week if possible.

There is little support for other pharmacological treatments beyond antipsychotics. There is no evidence to support the use of benzodiazepines in delirium outside of the context of delirium related to benzodiazepine or alcohol withdrawal, or in situations where antipsychotics are contraindicated, such as in dementia with Lewy bodies or Parkinson's disease. Benzodiazepines can trigger delirium, increase the risk of falls, and cause changes in memory and withdrawal symptoms (Cerveira et al, 2017). The 2015 Beers criteria do not recommend their use, and they are also not mentioned in the National Institute for Health and Care Excellence guideline. There is also no evidence for the use of acetylcholinesterase inhibitors in patients with delirium (Tampi et al, 2016).

Primary prevention

With limited evidence for pharmacological treatment and evidence suggesting that delirium is preventable in 30–40% of cases, the primary prevention of delirium has gained traction (Inouye et al, 2014). Multicomponent prevention strategies – including early mobilization, adequate hydration, sleep enhancement, orientation to time and place, therapeutic activities such as reminiscence, and hearing and vision optimization – have consistently demonstrated efficacy, and a meta-analysis by Hshieh et al (2015) reported a significant 53% reduction in delirium incidence and 62% reduction in falls with these interventions in older patients. Adopting a new culture of preventing delirium was stressed in the National Institute for Health and Care Excellence guideline (2010), and although these strategies are often nurse-led and commonplace on wards caring for older people, awareness of their efficacy is important.

Deprivation of liberty

Deprivation of liberty safeguards were first introduced in 2009, with the purpose of securing independent professional assessment of (a) a person's capacity to make a decision about remaining in the hospital/care home for care/treatment, and (b) whether it is in their best interests to be detained. The scope for needing deprivation of liberty safeguards was significantly widened after the UK Supreme Court's (2014) judgement in Cheshire West and Chester Council *vs* P case, and this has been reflected by the number of applications for deprivation of liberty safeguards (*Figure 1*).

The reason for an individual's placement and his/her compliance was deemed not relevant, and instead an 'acid test' was described for what may constitute a deprivation of liberty: namely, a person who 'lacks capacity to consent to their care/treatment arrangement' and who is under 'continuous supervision and control and not free to leave'. This is relevant to many patients with delirium, but a deprivation of liberty safeguards application is only needed when the deprivation is for a 'non-negligible period of time'.

Subsequent case law suggests that this length of time varies significantly depending upon the nature and intensity of the particular circumstances (British Medical Association, 2018) and individual trusts may provide further guidance on this issue. A deprivation of liberty safeguards application can be self-authorized for up to 7 days by following the 'urgent authorisation' process, which is often needed as a delay in the response to a deprivation of liberty safeguards applications is well recognized.

TOP TIPS

- Prescribe antipsychotics as stat medications as opposed to 'as required'.
- Beware of the negative effects of benzodiazepines, including triggering delirium.
- Family members often elicit a more positive response from patients than doctors do.
- Consider a deprivation of liberty safeguards application for all patients suffering from delirium.

Conclusions

Delirium is a common condition. Pharmacological interventions should be restricted to cases where patients are in distress and at risk of harming themselves or others. Non-pharmacological multifactorial strategies to prevent delirium should be emphasized, especially given the potential long-term implications of delirium, such as accelerated cognitive decline. **BJHM**

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KEY POINTS

- Pharmacological treatments for delirium may have a benefit, but this is inconclusive, and there are associated risks.
- Antipsychotics should only be used when a patient is in distress and poses a safety risk to him-/herself or others, after verbal and non-verbal de-escalation techniques have already been tried.
- Haloperidol 0.5 mg or olanzapine 2.5 mg are reasonable initial doses for delirium as the response can vary significantly by patient.
- A collateral history for knowledge of the patient's baseline and the timeline of decline are important in diagnosing delirium.
- Strategies to prevent and treat delirium need to be multi-factorial, as often there are many precipitating causes.