Delirium: Diagnosis, Aetiopathogenesis and Treatment

Delirium is a richly varied syndrome of cognitive and behavioural features which may co-exist with other somatic and mental disorders. As there is currently no diagnostic test and no reliable biomarkers have yet been identified, delirium remains a clinical diagnosis. A high index of clinical suspicion may be required in order to make the diagnosis, which should probably be considered in any patient labelled as confused (a term frequently used but with variable meaning), vague, uncooperative, rambling, agitated, or unable to give a coherent history.

Diagnosis and differential diagnosis
Both the Diagnostic and Statistical Manual (DSM) and the International Classification of Diseases (ICD) have diagnostic criteria for delirium.

DSM-IV-TR recognises four diagnostic categories:
- Delirium due to a medical condition
- Substance-induced delirium: due to intoxication or withdrawal
- Delirium due to multiple aetiologies
- Delirium not otherwise specified

Three common diagnostic criteria are required:
- Disturbance of consciousness:
  - This may encompass both quantitative and qualitative aspects of consciousness, hence “level” (= arousal, alertness, vigilance) and “intensity” (= selective attention) of consciousness; reduced clarity of awareness of environment; reduced ability to focus, sustain, or shift attention. Disordered attention may be evident clinically as increased distractibility.
- Change in cognition:
  - This may manifest as disorientation, language disorder, memory deficit, perceptual disturbance (illusory, hallucinations). These features should not be better accounted for by dementia.
- Development/Course:
  - Onset over a short period of time (hours, days) with fluctuation during the course of the day. Disturbance of sleep/wake cycles is typical, often with worsening of symptoms at night (“sundowning”).

In addition there may be diagnostic criteria by category, based on evidence from the clinical history, examination, or investigations, of a general medical condition; substance intoxication, medication use related to disturbance; more than one aetiology; or insufficient evidence for any of the above.

In ICD-10, the requirements for diagnosis are similar, and include:
- Impairment of consciousness and attention
- Global disturbance of cognition
- Psychomotor disturbance
- Disturbance of sleep–wake cycle
- Emotional disturbances

A brief consideration of these diagnostic criteria will indicate the potential clinical heterogeneity of delirium. However, two principal subtypes of delirium are described: the less common, but more easily recognised, is characterised by agitation or hyperactivity. The more common, but insidious, “quiet” variant, characterised by hypactivity, withdrawal, and apathy, may be easily overlooked and/or misdiagnosed as depression. Not surprisingly, it is the latter form of delirium which has a poorer outcome.

Rating scales have been developed which may be helpful in screening for the diagnosis, such as the Delirium Rating Scale (DRS), the Confusion Assessment Method (CAM), and the Neecham Confusion Scale (NCS); or for measuring the severity of delirium, such as the Confusional State Evaluation (CSE) and the Delirium Severity Scale (DSS).

The differential diagnosis of delirium includes:
- Dementia
- Aphasia (especially Wernicke’s aphasia)
- Psychiatric disorders:
  - schizophrenia
  - depression/mania
  - attention deficit disorder

Many texts include tables which list the factors differentiating delirium from dementia, for example in terms of onset (acute vs. insidious), course (fluctuating vs. stable), and duration (hours/days vs. months/years). However, it is of crucial importance to recognise that the two conditions show significant overlap, dementia being an important predisposing factor for the development of delirium, and delirium sometimes being the presenting feature of dementia. In any elderly person developing delirium, the possibility of an underlying diagnosis of dementia must be considered. However, meaningful assessment of cognitive functions to confirm or refute a diagnosis of dementia cannot be undertaken whilst delirium persists, because of the impairments of consciousness and attention.

Epidemiology, aetiology, pathogenesis, investigation
Delirium is common, more so in hospital in-patients (the subjects of the majority of studies) than in the community. In medical in-patients, prevalence of delirium may be 10-20%, and incidence 5-10%. In surgical patients, the incidence may be up to 30%. Certain types of surgery seem particularly associated with delirium, especially cardiac and orthopaedic (especially hip fracture surgery).

Studies have identified a number of factors which may contribute to the aetiology of delirium. These may be conveniently classified as predisposing and precipitating factors.

Predisposing factors include:
- Age: frailty, physiological age, rather than chronological age per se
- Sex: men > women
- Neurological illness: dementia
- Burden of co-morbidity; dehydration
- Drugs: especially anticholinergics
- Visual, hearing impairment

Precipitating factors include:
- Medications: benzodiazepines, opiates
- Intercurrent illness:
  - Infection: systemic, focal (CNS)
  - Metabolic: hypoglycaemia, hypoxia
  - CNS disorders: head injury, epilepsy, inflammatory
- Iatrogenic events: surgery

A multifactorial model of pathogenesis suggests an inverse relation between pre-existing vulnerability (predisposing factors) and the severity of insult (precipitating factors) required to initiate delirium.

The pathophysiology of delirium is an area of much research. It is believed that diverse aetiologies may...
converge on a "final common neural pathway", involving in particular the prefrontal, parietal, and fusiform (especially right), cortices. The factors implicated include excessive stress response, mediated by the hypothalamo-pituitary-adrenal axis; imbalance of neurotransmitters, most particularly reduced acetylcholine and increased dopamine; and immunological factors such as cytokines (increased TNF-alpha, reduced IGF-1, somatostatin)4.

The aetiological formulation into precipitating and predisposing factors guides the approach to investigation. The aim should be to identify any possible precipitating factors, such as an underlying medical disorder (Box 1, above).

Treatment and Prognosis

Specific treatment may be instituted if delirium is diagnosed early and an underlying aetiology or precipitating cause is identified, such as a medical condition (infection, metabolic disturbance), substance misuse, iatrogenesis (use of certain medications).

More general measures must not be overlooked, such as maintenance of fluid intake and nutrition. If spectators and/or hearing aids are normally worn they should be provided, after ensuring that they are in working order, to minimise sensory deprivation and the potential for misinterpretation of sensory stimuli. Environmental modulation, to avoid under- or over-stimulation, is recommended5, but is often impractical on general medical and surgical wards. Relatives and friends may visit regularly, to encourage orientation. Sleep should not be disturbed if possible.

Drug therapy is not mandatory, with the possible exception of hyperactive patients who are deemed at risk of harm to themselves or others. There is currently little trial data to guide drug use. The options include neuroleptics, either traditional D2 receptor antagonists, such as haloperidol, or newer atypical antipsychotics; or benzodiazepines, such as lorazepam. The neuroleptics appear to be superior, and early regular low dose therapy may be beneficial, perhaps, to avoid under- or over-stimulation. The aetiological formulation into precipitating and predisposing factors guides the approach to investigation. The aim should be to identify any possible precipitating factors, such as an underlying medical disorder (Box 1, above).

Further Reading


References


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