

What is delirium in critical care?

Introduction

Imagine you are caring for a critically ill patient admitted with severe community-acquired pneumonia. Unfortunately, this evolves rapidly with severe sepsis that results in both cardiovascular and respiratory failure. You know the patient has haemodynamic failure because you are monitoring the blood pressure and heart rate. You know the patient has respiratory failure because you are monitoring the respiratory rate and the oxygen saturation. You treat the patient with antibiotics, ventilatory support, fluids and inotropes.

He gets better, a job well done.

But what about the brain?

Just like the other organs, the brain can acutely fail in critical illness. An acute episode of brain failure is recognized as delirium. Delirium is an acute organ failure, and can happen in critical care, the general ward or the community at large. It is common; it is dangerous, even life-threatening. It is all the more dangerous because we know little about it. Its importance has been underestimated in the critically ill

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patient. The delirious patient is in an acute confusional state with a fluctuating altered mental status, inattention, an altered level of consciousness, disorganized thinking and often will have hallucinations. The delirium is triggered by an acute medical event, related to drugs or illness.

We therefore need to monitor the brain!

We monitor the patient's organs so we will know how they are functioning and when they are failing. If we do not monitor the brain how will we know if it fails?

But how can we do so?

Any critically ill patient who responds to a verbal stimulus such as calling their name can be screened for delirium in less than 2 minutes whether intubated or not, on or off sedation.

Delirium is a clinical syndrome and is diagnosed at the bedside, but it is not always easy to recognize. The majority of delirious patients are not agitated, pulling at lines and tubes, climbing out of bed; in fact they are lethargic and sleepy. If you want to know if your patient's brain is healthy you will need to check for function.

Fortunately this is quick and easy.

Does it affect the outcome?

Back to our patient with respiratory failure, 4 months later. He attends the follow-up clinic with his wife. His wife reports that

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he can't concentrate; he keeps forgetting friend's names, even those he has known for years. He can't remember where he has left things; all his vitality seems to have gone. Cardiovascular and respiratory functions are back to normal. Heart and lungs cured, brain irreversibly damaged. . .

Recognizing delirium allows initiation of treatment

Delirium is associated with serious adverse outcomes including death; your delirious patient is a medical emergency.

History

One syndrome, delirium, has been given many names. While Hippocrates is credited with the first description of delirium even he used about 16 different words! Amongst them were *phrenitis* (or frenzy) and *lethargus* and he described patients that would oscillate between the two delirious states. In today's terminology these are now called hyperactive, hypoactive and mixed motoric subtypes. Hippocrates also noted that patients were often fidgety, plucking at the air and at their bedclothes. Clinical signs observed nearly 2500 years ago are still present today – just the bedclothes are different!

The word delirium appears for the first time in *De Medicina*. This document is what is left of a large encyclopaedia compiled by Celsus, a Roman living under the reign of Tiberius (around AD 1). It was only rediscovered around 1480 in Milan. *De Medicina* was soon widely published, and

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Figure 1.1 Aulus Cornelius Celsus, *De Medicina*, 1478, Florentine. Courtesy of the Historical Medical Library of The College of Physicians of Philadelphia.

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became one of the most important ancient sources for Renaissance medicine. Celsus used the word delirium to describe mental disorders during fever or head trauma. He reported that wine could be used as part of the treatment when not associated with fever (recognizing alcohol dependence as a possible cause of delirium). The word delirium derives from the Latin *deliro*–*delirare* that literally means going off track, a sharp description of a wandering brain!

The historian Procopius comes next and has left us a precise description of delirium during the bubonic plague when reporting about a possible epidemic in Constantinople in AD 542:

For there ensued with some a deep coma, with others a violent delirium, and in either case they suffered the characteristic symptoms of the disease. For those who were under the spell of coma forgot all those who were familiar to them and seemed to lie sleeping constantly . . . those who were seized with delirium suffered from insomnia and were victims of a distorted imagination.

It was not until the early 1800s that Greiner suggested that clouding of consciousness was the main pathogenic feature of delirium. This led Hughlings Jackson to define consciousness at the turn of the last century, as one function of the central nervous system that could be disturbed by different agents leading to positive and negative signs of disturbance.

Engel and Romano were the first to show that the reduction in the level of consciousness seen in delirious patients could be correlated to electroencephalogram (EEG) activity. This ‘unifying’ interpretation was based on

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psychopathological characteristics and concluded that the disturbance in consciousness results in the failure of different cognitive tasks, fluctuating levels of awareness, psychomotor hyper- or hypoactivity, agitation or lethargy. In 1959 they complained that clinicians were ill-equipped to recognize delirium and that more should be done to train them to recognize the problem. They declared that a physician's concerns are to 'protect the functional integrity of the heart, liver and kidneys of his patient but has not learnt to have similar regard for the functional integrity of the brain'.

Dr Lipowski, a Polish-born, Irish-trained psychiatrist who settled in North America, proposed a definition of delirium in 1990 that has been very influential in the most recent psychiatric classifications. Delirium is 'a transient, global disorder of cognition, consciousness and attention regardless of the level of consciousness (awareness) or psychomotor activity that a given patient exhibits which may often change from one extreme to another in the course of a single day'; or a 'transient organic mental syndrome of acute onset, characterized by global impairment of cognitive functions, a reduced level of consciousness, attentional abnormalities, increased or decreased psychomotor activity and disordered sleep-wake cycle' (adapted from Lipowski [1]).

Other recent key players include Dr Sharon Inouye, who developed the Confusion Assessment Method, and Dr Paula Trzepacz working in key areas of phenomenology and neuropathogenesis.

Throughout history delirium has been described as a serious clinical condition with a poor prognosis. Hippocrates noted

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'cases of silent delirium, with restlessness, a changing gaze . . . are likely to prove fatal'. Also delirium associated with gnashing meant almost certain death. Philip Barrough in 1593 noted that it is an incurable and deadly condition in most cases. Importantly he added that, in the rare cases where it did resolve, it might be followed by memory loss and an inability to reason.

Classification

In the 1970s the American Psychiatric Association developed the *Diagnostic and Statistical Manual of Mental Disorders*, better known as DSM, to provide diagnostic criteria for mental disorders. Updated versions have been published, and these will continue to evolve as new data from research and clinical experience emerge. The latest is the DSM-5 in which delirium and all subtypes of dementia are classified under cognitive disorders, the unifying feature being a primary clinical deficit in cognitive function, acquired rather than developmental.

The alternative *International Classification of Diseases* (ICD) by the World Health Organization (WHO) has a broader remit as the international standard diagnostic classification for all general epidemiological use, many health management purposes and clinical use. It is now at its tenth revision (ICD-10). The next one, ICD-11, is due around 2016.

Regarding delirium the ICD-10 is overall similar to the DSM-5. Both are classifications of mental disorders based on diagnostic criteria, i.e. history, examination and clinical tests, and were first compiled from a need to bring order to the

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Table 1.1 Diagnostic criteria for delirium

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1. Disturbance of consciousness: Reduced clarity of awareness of the environment with reduced ability to focus, sustain or shift attention
 2. A change in cognition: Memory deficit, disorientation, language disturbance or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia
 3. Develops over a short period of time and fluctuates: Usually hours to days. Tends to fluctuate during the course of the day
 4. There is evidence that the disturbance is caused by the direct physiological consequences of a general medical condition. History, physical examination or laboratory finding
 5. Patient is not in a severely reduced level of arousal equivalent to being comatose
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chaotic psychiatric terminology, a result of the different theoretical models and ‘schools’ of thought that have existed for a long period.

Medical literature on delirium almost always quote DSM-IV criteria as a reference standard for the diagnosis. Shortly before the publication of DSM-5, the US National Institute of Mental Health made a decision to move away from clinical checklist DSM criteria, to a research framework they have developed (Research Domain Criteria). The rationale is to look beyond symptoms alone and collect genetic, imaging, physiological and cognitive data.

DSM-5 criteria

The DSM-5, the fifth edition, was published in May 2013. There are five diagnostic criteria, against four in the fourth edition.

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Starting with a disturbance of attention, 'i.e. to direct, focus, sustain or shift attention' (or more simply, inattention), which develops within a short time and fluctuates. This is combined with an additional disturbance of cognition, e.g. memory loss, disorientation, language disturbance; or a perceptual disturbance, such as hallucinations or delusional thoughts, not known to be caused by another cognitive disorder such as established or developing dementia. Delirium cannot be established as present in a patient with a severely reduced level of arousal, i.e. comatose. While in practice hallucinations are relatively common in delirium they are not needed for the diagnosis. Finally there must be clinical evidence that there is a medical cause or causes, either illness, toxin or drug related.

After establishing that a patient fulfils these criteria the DSM classifies delirium into groups dependent on the presumed cause and specifies it as substance intoxication or withdrawal, medication induced, due to another medical condition – the name of which should be noted – or delirium due to multiple aetiologies, which is the section most likely to apply to critically ill patients. Further useful information is whether the delirium is acute, i.e. lasting days, or persistent, and hyperactive, hypoactive or mixed (see Chapter 3).

New to DSM-5, so absent from DSM-IV, is the criterion that the disturbances of attention and change in cognition should not be present in a patient with severely reduced level of arousal 'such as coma'. Importantly, the accompanying text notes that some patients with a reduced level of arousal, as is typical in delirium, may only show minimal responses such that they are incapable of engaging with assessment of

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attention. DSM-5 determines that this inability to engage is severe inattention, which, combined with the low-arousal state, indicates the patient has delirium. This is seen in critically ill patients who, while they will open their eyes, do not squeeze your hand on request at all for assessment of delirium (see Chapter 7).

It is important to note that whilst guidance is given regarding differentiation of delirium from dementia, patients with dementia are particularly vulnerable to delirium, presenting with delirium superimposed on top of dementia.

Terminology in critical care

In 1990, over 30 terms used to refer to delirium were identified in the medical literature (Figure 1.2). It is tempting to bring back terms such as ‘subacute befuddlement’ or maybe ‘dysergastic reaction’ but of course it is unlikely this would lead to intensivists taking delirium more seriously. Critical care lent its name to ICU psychosis and ICU syndrome, often to allow the delirium to be dismissed as an expected and inconsequential complication of critical illness. Other names, such as septic encephalopathy, hepatic encephalopathy, toxic confusional state, acute confusional state, metabolic encephalopathy or acute brain syndrome, highlight how important the syndrome is *in these situations*. But no delirium can be supposed benign or self-limiting.

The failure to standardize terminology may be one reason why delirium has not been given to date the scientific consideration it deserves, even if the multiplicity of terms and