INTRODUCTION

Cognition can be defined as the mental activities involved in acquiring and processing information.

That is, the mental processes required for everyday living. It enables the individual to solve problems, make plans, and is not the same as intelligence. Changes in cognition are commonly categorized into three distinct clinical conditions; delirium, postoperative cognitive decline (POCD), and dementia according to the timing and duration of symptoms ***(Ely et al., 2004).***

In terms of patient-related baseline factors, or sometimes called predisposing factors, increasing age and lower levels of education have been identified as the main ones in the early study by the International Study on Postoperative Dysfunction (ISPOCD) ***(Henderson et al., 2009).***

In addition to predisposing risk factors, numerous potential precipitating risk factors for POCD have been investigated. The early ISPOCD study reported that the duration of anesthesia, a second operation, postoperative infections, and pulmonary complications increase the risk of POCD ***(Newman et al., 2006).***

Genetic studies from have demonstrated a relationship between certain genotypes and the risk of dementia and cognitive decline. Specifically, elevated risk of Alzheimer's has

been demonstrated among individuals with the E4 allele of the apolipoprotein E (APOE) gene in many populations ***(Maestre et al., 2008).***

Despite the earlier studies that POCD is prevalent after cardiac surgery, studies in patients who underwent cardiac surgery without the use of cardiopulmonary bypass did not demonstrate a lower incidence of POCD, despite a smaller embolic load in the middle cerebral artery measured by Doppler in patients undergoing off-pump surgery ***(Jensen et al., 2008).***

Prevention of cognitive change is the most effective way to reduce its complications. However, many predisposing factors, such as age, chronic illness, and pre-existing cognitive impairment, cannot currently be modified acutely ***(Patel et al., 2009).***

Treatment of Postoperative cognitive dysfunction is either non-pharmacological like: review the delirium risk factors looking for precipitant causes that may be correctable. Some of the risk factors listed are clearly more amenable to modification than others ***(Ely et al., 2004).***

The mainstay of pharmacological therapy and that recommended by both the Intensive Care Society and the American College of Critical Care Medicine is haloperidol ***(Borthwick et al., 2006).***

Aim of the Essay

The aim of this essay is to focus the light on the incidence and diagnosis, risk factors, potential mechanisms and prevention and treatment of POCD.

INCIDENCE AND DIAGNOSIS OF POCD

Cognition and cognitive change;

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That is, the mental processes required for everyday living. It enables the individual to solve problems, make plans, and is not the same as intelligence. Changes in cognition are commonly categorized into three distinct clinical conditions; delirium, postoperative cognitive decline (POCD), and dementia according to the timing and duration of symptoms (Fig. 1) ***(Ely et al., 2004).***

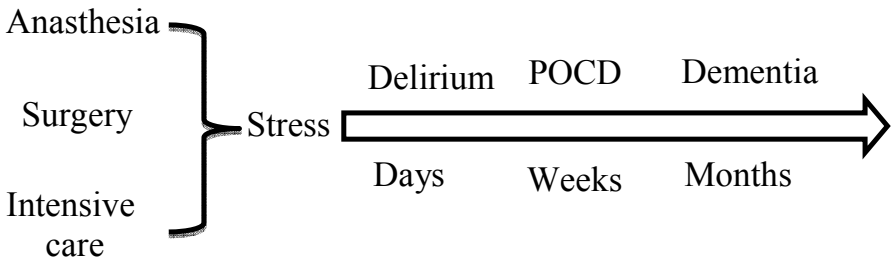


Fig. (1): Triggers and timeline of postoperative cognitive change ***(Ely et al., 2004).***

Delirium

Any acute disturbance of the state of mind should be described as delirium. The syndrome is defined in the Diagnostic

and Statistical Manual of Mental Disorders IV (DSM IV) as an acute onset fluctuating change in mental status characterized by a reduced awareness of the environment and disturbance of attention.

DSM IV further sub-classifies the delirium according to cause;

i) Due to a general medical condition.

ii) Substance-induced delirium; the cause of anesthesia emergence delirium ***(Bruce et al., 2007).***

iii) Delirium due to multiple etiologies

iv) Delirium not otherwise specified.

Frequently complicating the course of hospitalized patients, delirium can manifest as:

- Hypoactive seen in 64% of surgical intensive care unit ICU patients but often missed.
- Hyperactive 5-22% of cases.
- Mixed psychomotor behaviors ***(Bruce et al., 2007).***

DIAGNOSIS

Delirium is diagnosed by psychiatrists using DSM IV criteria. Whilst psychiatric referral can still be helpful, the

development of specific delirium assessment tools for use by the multi-disciplinary team has greatly improved its recognition on intensive care. However delirium is probably still under-diagnosed, particularly in the hypoactive sub-type, where the more subtle features may be overlooked. The assessment tool most commonly employed in UK clinical practice is the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) ***(Mac'Sweeney et al., 2010).***

Both CAM-ICU and the Intensive Care Delirium Screening Checklist (ICDSC) have been specifically validated for use on the intensive care unit. Appendices 1 & 2 illustrate how these assessment tools are conducted. Both are easy and quick to perform and have good inter-observer reliability. CAM-ICU, performed once every 24 hours, directly assesses the patient performing tasks to command and can be used during mechanical ventilation. ICDSC, documented every 8 hours, is more subjective as it relies on data collected during routine nursing care without direct assessment of the patient. Patients who are experiencing isolated hallucinations may be assessed as delirium negative by CAM-ICU but delirium positive by ICDSC ***(Plaschke et al., 2008).***

Appendix 1: Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) *(Lipowski 1983).*

Step 1 Level of consciousness: RASS

Scale	Label	Description
+4	Combative	Combative, Violent, immediate danger to staff
+3	Very Agitated	Pulls to remove tubes or catheters; aggressive
+2	Agitated	Frequent non-purposeful movements, fights ventilator
+1	Restless	Anxious, apprehensive, movements not aggressive
0	Alert & calm	Spontaneously pays attention to caregiver
-1	Drowsy	Not fully alert, but has sustained awakening to voice (eye opening & contact >10 sec)
-2	Light Sedation	Briefly awakens to voice (eyes open & contact <10 sec)
-3	Moderate Sedation	Movement or eye opening to voice (no eye contact)

VOICE

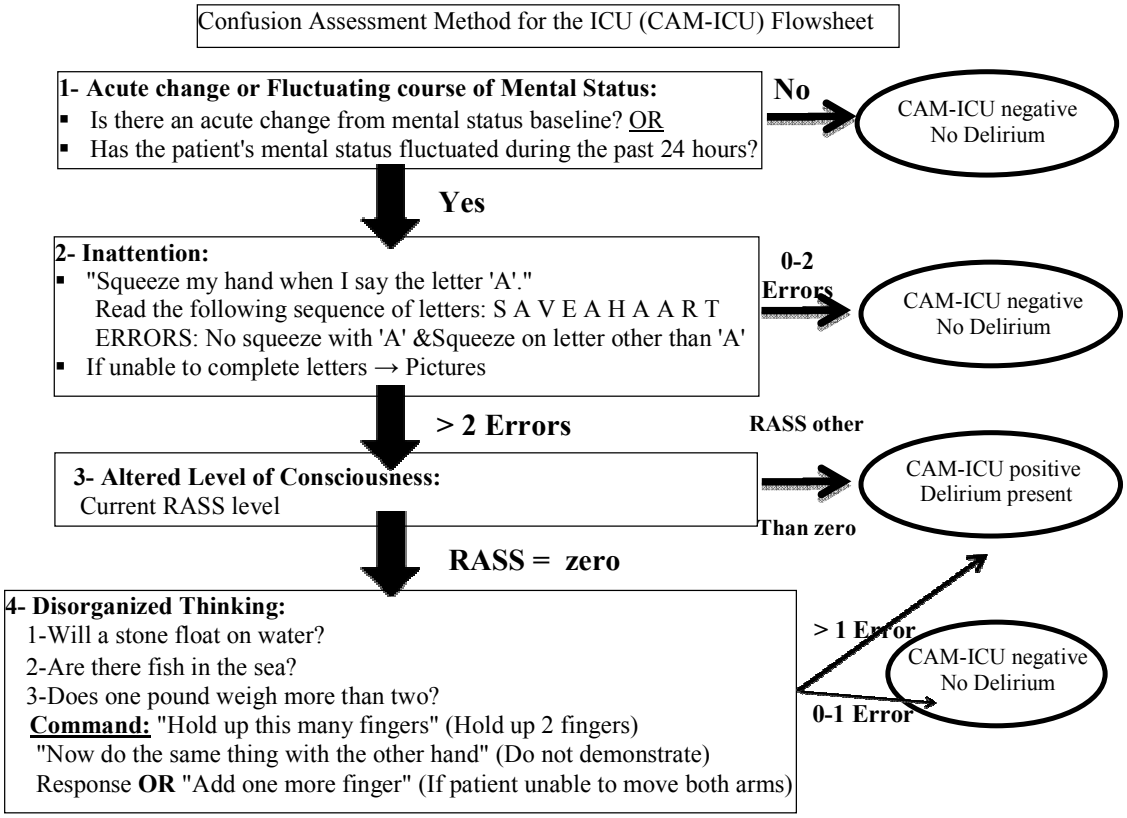
If RASS is ≥ -3 Proceed to CAM-ICU (Is patient CAM-ICU positive or negative?)

-4	Deep sedation	No response to voice, but movement or eye opening To physical stimulation
-5	Unarouseable	No response to voice or physical stimulation

TOUCH

If RASS is -4 or -5 → Stop (patient unconscious). Recheck later

Step 2 Content of consciousness: CAM-ICU



Appendix 2: Intensive Care Delirium Screening Checklist ***(Bergeron et al., 2010).***

Level of consciousness	Response	**Score**
A	No response	None
B	Response to intense and repeated stimulation (loud voice and pain)	None
C	Response to mild or moderate stimulation	1
D	Normal wakefulness	0
E	Exaggerated response to normal stimulation	1

SCORING SYSTEM:
The scale is completed based on information collected from each entire 8-hour shift or from the previous 24 hours. Obvious manifestation of an item = 1 point. No manifestation of an item or no assessment possible = 0 point. The score of each item is entered in the corresponding empty box and is 0 or 1.
1.Altered level of consciousness: **A** No response **B** The need for vigorous stimulation in order to obtain any response signified a severe alteration in the level of consciousness precluding evaluation. If there is coma (A) or stupor (B) most of the time period then a dash (-) is entered and there is no further evaluation during that period. **C** Drowsiness or requirement of a mild to moderate stimulation for a response implies an altered level of consciousness and scores 1 point. **D** Wakefulness or sleeping state that could easily be aroused is considered normal and scores no point. **E** Hypervigilance is rated as an abnormal level of consciousness and scores 1 point.
2. Inattention: Difficulty in following a conversation or instructions. Easily distracted by external stimuli. Difficulty in shifting focuses. Any of these scores 1 point.
3. Disorientation: Any obvious mistake in time, place or person scores 1 point.
4. Hallucination, delusion or psychosis: The unequivocal clinical manifestation of hallucination or of behavior probably due to hallucination (e.g. trying to catch a non-existent object) or delusion. Gross impairment in reality testing. Any of these scores 1 point.
5.Psychomotor agitation or retardation: Hyperactivity requiring the use of additional sedative drugs or restraints in order to control potentially dangerousness (e.g. pulling out IV lines, hitting staff). Hypo activity or clinically noticeable psychomotor slowing. Any of these scores 1 point.
6.Inappropriate, disorganized or incoherent speech: Inappropriate display of emotion related to events or situation. Any of these scores 1 point.
7. Sleep/wake cycle disturbance: Sleeping less than 4 hours or waking frequently at night (do not consider wakefulness initiated by medical staff or loud environment). Sleeping during most of the day. Any of these scores 1 point.
8.Symptom fluctuating; Fluctuation of the manifestation of any item or symptom over 24 hours (e.g.

INCIDENCE

Peterson et al. noted that the most common delirium subtypes were mixed (54.9%) and hypoactive (43.5%) whilst

hyperactive was found to be relatively uncommon (1.6%) ***(Peterson et al., 2006).***

Rudolph et al. reported a 5.4% attrition rate for evaluations performed between 7 and 21 days after noncardiac surgery; 19% for evaluations between 22 days and 132 days; and 17% for evaluations beyond 6 months postoperatively ***(Rudolph et al., 2008).***

CAM-ICu; The pilot for the CAM-ICU assessment tool found a high incidence of 83.3% in 111 study patients. Subsequent studies using CAM-ICU suggest that the incidence varies between 41-74%.This is in comparison to the data from our local mixed surgical and medical ICU in which CAM-ICU screening detected delirium in 31.7% of patients at some point in their admission ***(Vanstone, 2009).***

For many years, the lack of a consistent definition for delirium that could be applied to intensive care patients hampered efforts to determine its incidence in this setting. The development of the two delirium screening tools discussed had gone some way to address this issue. However reported incidence still varies widely (16.1%-83.3%) depending on the patient ***(Ely et al., 2010).***

During validation of the ICDSC, psychiatrists identified delirium in 16.1% of 93 study patients using DSM IV criteria ***(Bergeron, 2012).***

Cognitive function and critical illness

There are many procedural issues that should be considered when administering a neuropsychological protocol for the purpose of detecting POCD ***(Rasmussen et al., 2009).***

Test selection should be guided by choosing tests that have validity for detecting change in functioning in those domains of expected to be negatively affected by the surgical experience. In addition, there are several practical issues that should be considered when choosing tests for the assessment of POCD. For example, it is important to choose tests with difficulty levels that do not result in floor effects (many subjects scoring the lowest score possible) or ceiling effects (many subjects scoring the highest score possible**)** ***(Funder et al., 2010).***

Tests that do not have floor or ceiling effects are likely to have greater sensitivity to detecting a change in functioning associated with surgery. Choosing tests with parallel versions reduces potential practice effects from remembering test stimuli from earlier administrations. This is particularly problematic for word-list learning tasks because some subjects are able to recall words from a prior administration of the task. The parallel versions should be administered in a different order between subjects (e.g. ordered according to a Latin-square design) to avoid a potential form by occasion bias in results ***(Sands et al., 2009).***

Tests should be validated for the language in which they will be administered. For example, the difficulty of word list generation tasks that require the subject to list as many words as possible that begin with a specific letter varies depending on the letter specified ***(Borkowski et al., 1967).***

Difficulty levels will vary across languages for the same letter. Administration of tests used to detect POCD should be standardized across occasions and subjects. Consensus recommendations include that testing be conducted by "the same suitably qualified and trained individual and that the tests minimize subjectivity and be performed in a standardized manner." ***(Murkin et al., 2005).***

Although a variety of scoring methods for the detection of POCD have been used across studies, investigators generally agree that scoring methods should consider; 1) baseline performance, 2) practice effects, and 3) change on more than one neuropsychological test ***(Rafnsson et al., 2007).***

Baseline assessments allow determination of whether an actual change in cognitive functioning occurred subsequent to the surgical event. Nearly half of studies of POCD have been conducted in adults undergoing cardiac surgery, a population at risk for cognitive changes due to underlying heart or vessel disease ***(Rafnsson et al., 2007).***

Practice effects refer to improvement in performance due to familiarity with test procedures and can occur in patients with and without existing cognitive impairment ***(Sands et al., 2009).***

Timing of Assessment for POCD

Postoperative cognitive dysfunction can be broadly divided into acute, intermediate and late or long-term changes. Specifically, acute POCD has been used to describe cognitive decline detected within one week after surgery, intermediate POCD for changes within 3 months, and long-term POCD for changes 1-2 years following surgery. However, the exact significance of detecting POCD at these various time points is unclear. The time interval at which a diagnosis of POCD holds the greatest clinical significance has not been determined nor have any studies invalidated the importance of conducting assessments at a specific time point ***(Duggleby and Lander, 2010).***

Early assessments of POCD likely capture a different phenomenon than what late assessments of POCD capture, and each are accompanied by a unique set of issues. Surgery related factors may affect test performance in the immediate postoperative period, including acute pain, the use of drugs, nausea, limited mobility, and fatigue ***(Duggleby and Lander, 2010).***

Thus, it had been argued that patients should not be evaluated for POCD until at least one week postoperatively. this delay might be arbitrary, as negative outcomes are associated with POCD detected in the first week after surgery ***(Wang et al., 2007).***

Patients undergoing noncardiac surgery, POCD detected at hospital discharge (mean duration of stay, <7 days) was associated with an increased risk of death within the first 3months after surgery ***(Rasmussen et al., 2009).***

It has been reported that the average length of stay of patients over 50 years of age who underwent major noncardiac surgery with no postoperative complications was 4 days ***(Rohan et al., 2005).***

If patients experiencing cognitive decline are more likely to decline assessment, this selective attrition will bias study results toward the null, obscuring the detection of cognitive changes postoperatively ***(Rohan et al., 2005).***

POCD assessments that occur in the immediate postoperative period are important for elucidating the relationship between POCD and delirium. Because POCD and delirium both feature deficits in attention, whether they are related events on a continuum or distinct conditions remains unclear. In a retrospective analysis of the International Study for Postoperative Cognitive Dysfunction (ISPOCD) research data,