Post-operative delirium

Best practices for prevention and management

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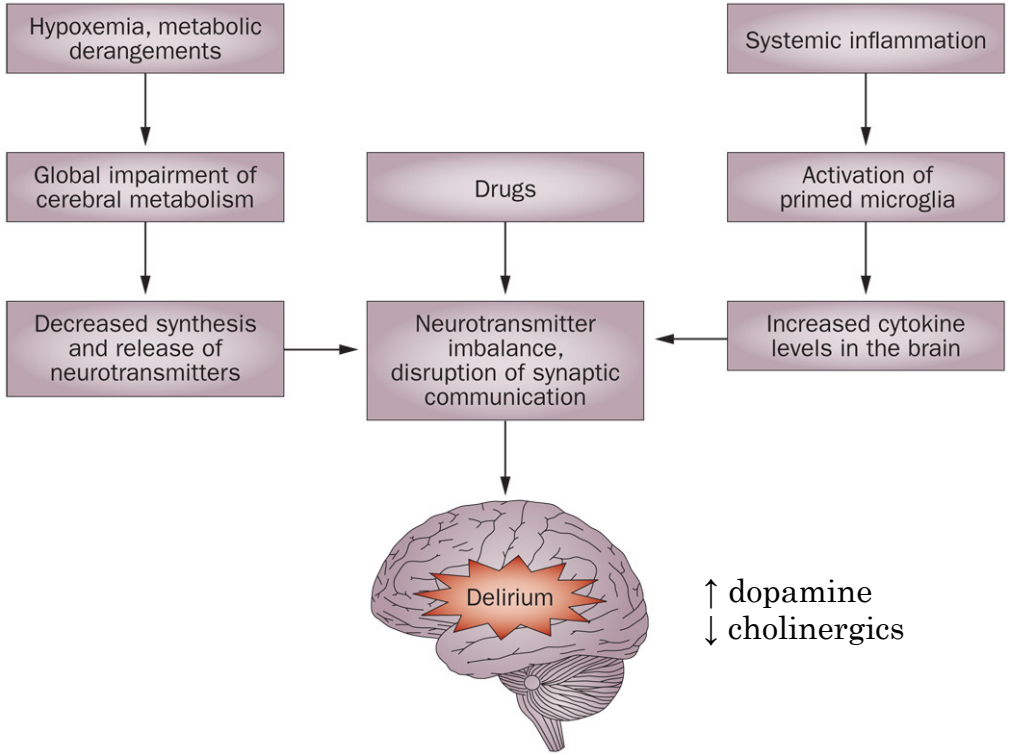
Agenda

Definition & detection	5min
Risk factors & prevention	10min
Dementia risk after delirium	10min
Questions	5min

Delirium

- Acute and fluctuating disturbance in attention and cognition, which is not based on a pre-existing neurocognitive disorder
- Postoperative neurocognitive disorders (NCDs) are a spectrum containing:
  a. Post-operative delirium (POD)
  b. Delayed neurocognitive recovery
  c. Postoperative cognitive dysfunction (POCD)
- Delirium superimposed on dementia (DSD) is also an emerging term (prevalence of 31% in a 2017 cohort study[1] and as high as 48.9% in hospitalized patients[2])
- NCDs affect 10-50% of surgical patients, who have increased mortality, longer lengths of stay, higher 30-day readmissions[3]



Source: Fong et al, 2009[4]

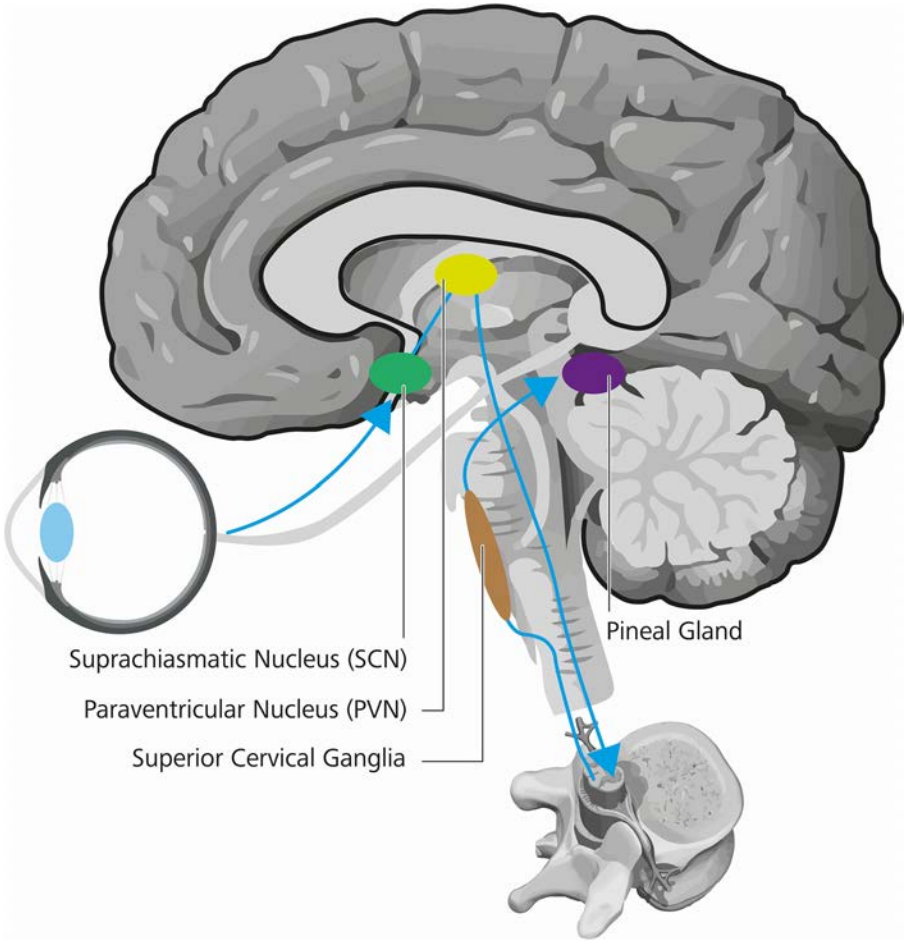
Feature	Delirium	Dementia due to Alzheimer disease	Frontotemporal lobe dementia	Diffuse Lewy body disease	Vascular dementia
Descriptive features	Inattention, impairment of immediate memory	Memory impairments, plus impairments in multiple other cognitive domains	Behavioural disorder, mental rigidity, distractibility	Fluctuating cognition with variations in attention and alertness	Abrupt deterioration or stepwise progression of cognitive deficits; mood and personality changes
Onset	Acute, episodic	Insidious	Insidious	Insidious	Insidious, abrupt or stepwise
Duration	Hours to months	Months to years	Months to years	Months to years	Months to years
Course	Fluctuating, might be worse at night and on waking	Chronic, progressive	Chronic, progressive	Chronic, progressive	Chronic, progressive
Alertness	Altered	Normal	Normal	Fluctuates	Normal
Reversibility	Usually	No	No	No	No
Attention	Impaired by definition	Usually, normal, but might be impaired in later stages	Might be persistently impaired and early feature	Fluctuates	Might be persistently impaired and early feature
Orientation	Fluctuates	Not oriented	Typically intact	Variable	Variable
Speech	Incoherent speech	Word-finding difficulties	Altered speech output; stereotypy of speech; echolalia; perseveration; mutism	Hypophonic speech	–
Thought	Disorganized and disconnected thoughts, for example, 'flight of ideas'	Difficulty with abstract thinking	Poor judgement; impulsivity	–	Abnormal executive function, including mental rigidity and poor insight and judgment
Perception	Distorted: illusions, delusions and/or hallucinations (often visual, tactile or poorly formed)	Delusions of theft or persecution, more common in later stages; hallucinations (auditory, distinct) uncommon	Delusions might be paranoid, religious or bizarre in nature	Visual hallucinations are recurrent and typically well-formed and detailed (that is, animals or children); delusions are common	Delusions more common in later stages
Psychomotor changes	Frequent	Inconsistent	Hyperorality; utilization behaviour	Parkinsonism	Psychomotor retardation
Agitation	Occurs with delirium symptoms, throughout the day	Might occur with sundowning or when resisting activities of daily living	Common	Variable	Variable
Sleep–wake cycle	Often reversed	Might be fragmented but circadian rhythmicity retained	Severely fragmented	REM sleep behaviour disorder	Sleep disturbances are common

Adapted from Table 1: Fong & Inouye, 2022[1]

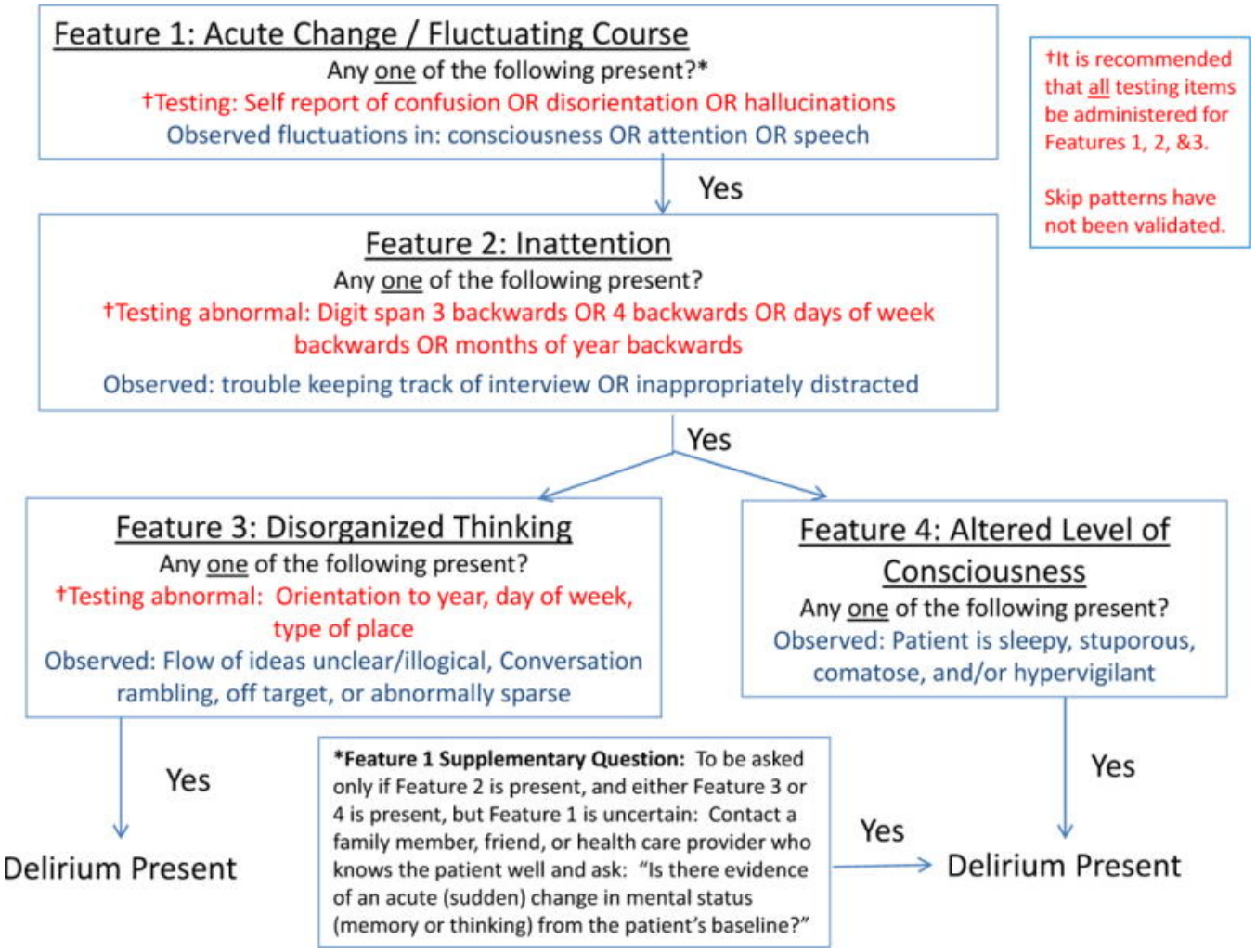
Sundowning

The emergence or worsening of neuropsychiatric symptoms (NPS) in the late afternoon or early evening

- Behaviors include anxiety, agitation, aggression, pacing, wandering, resistance, screaming, yelling, visual and auditory hallucinations, etc
- Not a DSM-V diagnosis, though commonly acknowledged and treated (though very limited pharmacologic studies[1])
- Blurry distinction from delirium, except for reversion to normalcy in the morning, which is typically too brief a time course for delirium (which tends to last at least several days[2])



Source: Wahl et al, 2019[3]



3D-CAM (3min Confusion Assessment Method)[1]

Detecting delirium

- Hyperactive, hypoactive, and mixed subtypes
- 3D-CAM initial performance in patients with dementia (sensitivity 0.95, specificity 0.86)[1]
- Validated in an 18+ population (sensitivity 1.0, specificity 0.88, PPV 0.44, NPV 1.0)[2]

ADMINISTRATION OF 4-DSD

ITEM 1. ALERTNESS

Level of consciousness assessed with mRASS mRASS=_____ (If m-RASS score = -4 or -5 the patient cannot be assessed with the 4-DSD)	❒ =0 (0 points)	❒ ≠ **0** (1 point)

STEP 1 partial score ____/1

ITEM 2. ALTERED BRAIN FUNCTION

Inconsolability	○ Does the patient not respond to attempts at comfort? ○ Does the patient have repeated outbreaks, moans, etc?	❒ Yes ❒ Yes	❒ No ❒ No	❒ At least one yes (1 point)
Unawareness	○ Is the patient unaware of his surroundings, his personal effects, etc? ○ Does the patient not recognize or fail to interact with his caregivers?	❒ Yes ❒ Yes	❒ No ❒ No	❒ At least one yes (1 point)
Sleep-wake rhythm disorder	○ Does the patient feel asleep during the stimulation? ○ Does the patient sleep little during the night? ○ Is insomnia present? ○ Does the patient reverse the sleep/wake rhythm	❒ Yes ❒ Yes ❒ Yes ❒ Yes	❒ No ❒ No ❒ No ❒ No	❒ At least one yes (1 point)

STEP 2 partial score ____/3

ITEM 3. ATTENTION

Instructions:

- ○ Hold the image about 30 cm from the patient's face, moving it slowly to the right or left; show the 10 cards one at a time
- ○ Show the first card (mirror) moving it slowly to the right or left, saying: "LOOK AT THE MIRROR" (it is possible to repeat the instruction only one time)
- ○ Show the second card (image) moving it slowly to the right or left, saying: "LOOK AT THE CARD: IS IT AN ANIMAL"? Recording the answer (If the patient does not respond register as an incorrect response).
- ○ Repeat this operation by alternating image/mirror cards until all 10 cards have been shown

Eye Contact: does the patient maintain eye contact with the examiner or with the card?	❒ Yes (0 points)	❒ No (1 point)

4-DSD assessment for delirium[1]

Detecting delirium cont'

- Newer score 4-DSD
- For use in patients with an established diagnosis of moderate-to-severe dementia
- Range of 0-12, higher score indicates delirium
- 4-DSD $\geq$ 5 has ~80% sensitivity and specificity

Risk factors for delirium

Potentially modifiable

- Sensory impairment (hearing or vision)
- Immobilization (catheters or restraints)
- Medications (e.g., sedative hypnotics, narcotics, anticholinergic drugs, etc)
- Acute neurological diseases (e.g., acute stroke [commonly right parietal], intracranial hemorrhage, meningitis, encephalitis)
- Comorbid illness (e.g., infections, anemia, dehydration, poor nutritional status, fracture or trauma, HIV infection)
- Metabolic derangement
- Pain and/or emotional distress
- Environment (e.g. intensive care unit stay)
- Sustained sleep deprivation

Nonmodifiable

- Dementia or cognitive impairment
- Advancing age (>65 years)
- History of delirium, stroke, neurological disease, falls or gait disorder
- Multiple comorbidities
- Male sex
- Chronic renal or hepatic disease

Adapted from Box 1: Fong et al, 2009[1]

Risk Factors for Delirium

	General Medicine	Surgery		ICU
		Non-cardiac	Cardiac	
Predisposing factors	**Relative Risks**			
Dementia	2.3–4.7	2.8		
Cognitive impairment	2.1–2.8	3.5–4.2	1.3	
History of delirium		3.0		
Functional impairment	4.0	2.5–3.5		
Vision impairment	2.1–3.5	1.1–3.0		
Hearing impairment		1.3		
Comorbidity/severity of illness	1.3–5.6	4.3		1.1
Depression	3.2		1.2	
History of transient ischemia/stroke			1.6	
Alcohol abuse	5.7	1.4–3.3		
Older age	4.0	3.3–6.6		1.1
Precipitating Factors				
Medications				
Multiple medications added	2.9			
Psychoactive medication use	4.5			
Sedative-hypnotics				4.5
Use of physical restraints	3.2–4.4			
Use of bladder catheter	2.4			
Physiologic				
Elevated serum urea	5.1			1.1
Elevated BUN/creatinine ratio	2.0	2.9		
Abnormal serum albumin			1.4	
Abnormal sodium, glucose, or potassium		3.4		
Metabolic acidosis				1.4
Infection				3.1
Any iatrogenic event	1.9			
Surgery				
Aortic aneurysm		8.3		
Non-cardiac thoracic		3.5		
Neurosurgery				4.5
Trauma admission				3.4
Urgent admission				1.5
Coma				1.8–21.3

Inouye, et al 2014[1]

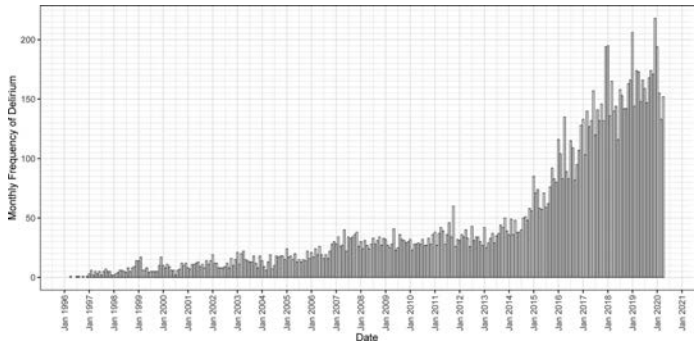
Cognitive risk after delirium

- Is delirium simply a marker of vulnerability to dementia, or does delirium itself leads to dementia?
- Early 2008 study found in 200 hip surgery patients age >60, 41 developed post-operative delirium (POD). 38 months after surgery, 53.8% of the POD patients suffered cognitive impairments vs 4.4% of non-delirious patients (OR 41.2)[1]
- 2014 Lancet review of delirium in the elderly (right). Delirium posed a cognitive risk in certain patient populations[2]

Population	Prevalence (range)[†], Incidence (range)	Outcomes (Adjusted Relative Risks[‡], RR)
Surgical		
Cardiac	- - - 11%-46%	Cognitive Dysfunction (RR=1.7) Functional Decline (RR = 1.9)
Non-Cardiac	- - - 13% - 50%	Functional Decline (RR = 2.1) Cognitive Dysfunction (RR = 1.6)
Orthopedic	17% 12% – 51%	Dementia/ Cognitive Dysfunction (RR = 6.4 – 41.2) Institutionalization (RR = 5.6)
Medical		
General Medical	18% – 35% 11% – 14%	Mortality (RR= 1.5 –1.6) Functional decline (RR = 1.5)
Geriatric Units	25% 20% – 29%	Falls (RR = 1.3) Mortality (RR = 1.9) Institutionalization (RR = 2.5)
Intensive Care	7%–50% 19% – 82%	Mortality (RR = 1.4 – 13.0) Longer LOS (RR = 1.4 – 2.1) Extended Mechanical Ventilation (RR = 8.6)
Stroke	- - - 10% - 27%	Mortality (RR = 2.0) Any of 3 outcomes: increased LOS, functional impairment, or death (RR= 2.1)
Dementia	18% 56%	Cognitive Decline (RR = 1.6–3.1) Institutionalization (RR = 9.3) Mortality (RR = 5.4)
Palliative Care/Cancer	- - - 47%	- - -
Nursing Home/Postacute Care	14% 20% - 22%	Mortality (RR = 4.9)
Emergency Department	8% - 17% - - -	Mortality (RR = 1.7)

Cognitive risk cont'

- 2021 meta-analysis of 6 studies (n=901) showed that delirium was associated with increased odds of developing new dementia compared to patients without delirium (OR 11.9, 95% CI 7.29-19.6)[1]
- 2022 cohort study of 12,949 patients documented cumulative incidence of dementia among patients who experienced an episode of delirium but who had not yet been diagnosed with dementia before that episode
  - Followed for average 741 days (min 0.5 to max 8855 days)
  - 27% (3530/12949) had diagnosis of dementia, 45% (5788) died without dementia, 28% (3631) were censored (i.e. alive/without diagnosis of dementia)
  - Concluded that a first episode of delirium after age 65 is associated with a 9% risk of developing dementia at 6 months, 13.6% at 1 year, and 31% at 5 years and a 49% of death (without dementia) at 5 years
  - Incidence of delirium diagnoses increased 1996-2020



Delirium Prevention Guidelines

- 2020 Consensus guidelines issued by the American Society for Enhanced Recovery & Perioperative Quality Initiative[1]
- Rationale being that up to 40% of delirium cases are potentially preventable[2]

Pre-hospital interventions to consider

- Identification of high-risk patients as part of pre-operative screening
- Addition of delirium as part of informed consent

STATEMENT	STRENGTH[A]	LOE[B]
We recommend hospitals and health systems develop processes to reduce the incidence and consequences of postoperative delirium through an iterative multidisciplinary quality improvement process.	Strong	D
We recommend that health care providers identify surgical patients at high risk for postoperative delirium.	Strong	C
We recommend that surgical patients identified as high risk for postoperative delirium be informed of their risk.	Weak	D
We recommend hospital and health systems develop a process to assess for postoperative delirium in older high-risk patients.	Strong	C
We recommend the use of multicomponent nonpharmacologic interventions for the prevention of postoperative delirium in older high-risk patients.	Strong	B
We recommend minimization of medications known to be associated with an increased risk of postoperative delirium in older high-risk surgical patients.	Strong	C
There is insufficient evidence to recommend using processed EEG monitoring in older high-risk surgical patients undergoing general anesthesia to reduce the risk of postoperative delirium.[c]	N/A	N/A
There is insufficient evidence to recommend specific anesthetic agents or doses to reduce the risk of postoperative delirium.	N/A	N/A
There is insufficient evidence to recommend regional/neuraxial blockade as the primary anesthetic technique to reduce the risk of postoperative delirium.	N/A	N/A
We recommend optimization of postoperative pain control to reduce the risk of postoperative delirium.	Weak	C
There is insufficient evidence to recommend administration of prophylactic medications to reduce the risk of postoperative delirium.	N/A	N/A
We recommend using ICU protocols that include sedation with dexmedetomidine to reduce the risk of postoperative delirium in patients requiring postoperative mechanical ventilation.	Strong	B

Sample of delirium trials

Failed

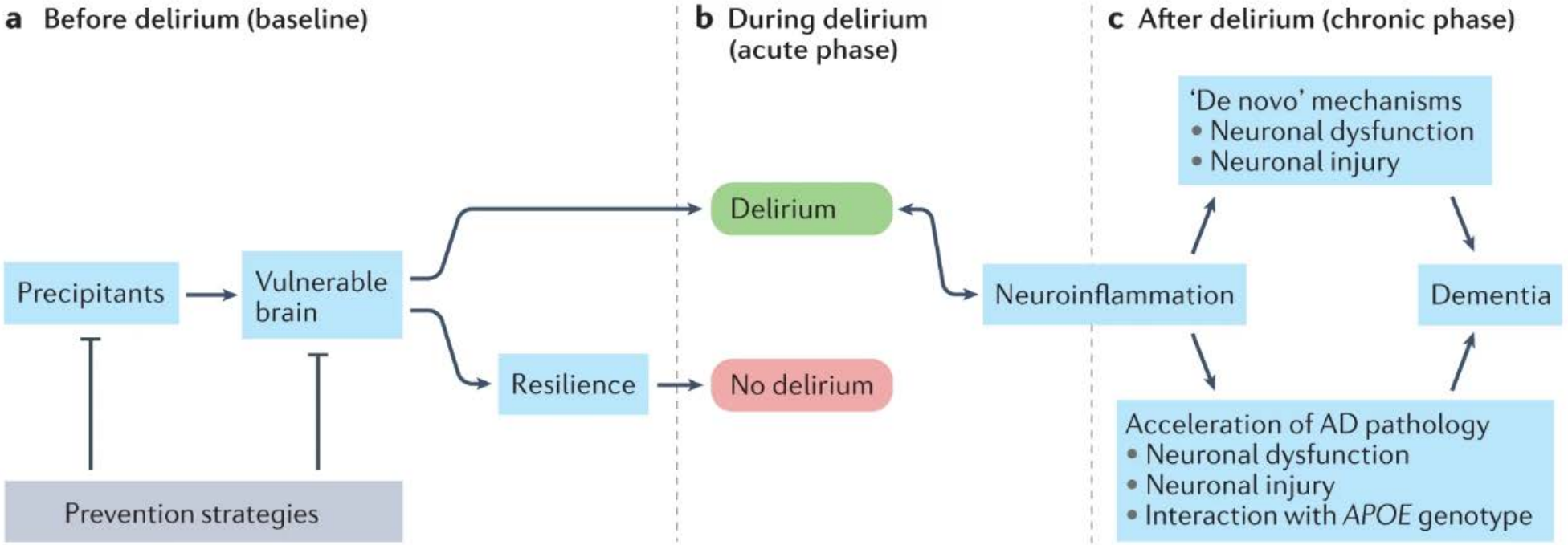
- Remelteon (RECOVER RCT), no benefit vs placebo in 80 older patients undergoing hip or knee replacement/revision[1]
- Haloperidol or 2nd generation antipsychotics (olanzapine, risperidone) have insufficient evidence to support efficacy in delirium prevention, or shortening delirium duration[2]
- Rivastigmine has been studied, initial results were promising but a later RCT was halted early due to increased mortality[3]

Ongoing

- EEG studies using spectral analysis (delta/theta/alpha bands) to diagnose delirium[4]
- Also intraoperative EEG monitoring with spectral data to guide anesthesia[5]
- Regional anesthesia instead of general to reduce delirium risk
- Flow velocity measurements with transcranial doppler (lower velocities observed in DSD)[6]

Fig. 1: A hypothetical model for the inter-relationship between delirium and dementia and potential opportunities for prevention.

From: The inter-relationship between delirium and dementia: the importance of delirium prevention



a,**b** | In the setting of precipitating factors, such as hypoxia, metabolic abnormalities, medications, infection or surgery, and in the presence of an existing vulnerability, such as Alzheimer disease (AD) or other neurodegenerative pathology, cerebrovascular disease, or injury, delirium (green) can occur. Alternatively, owing to the presence of resilience factors, such as cognitive reserve, or the implementation of prevention strategies (grey) to minimize one or more modifiable delirium risk factors, delirium does not occur (red). **c** | The development of delirium and subsequent neuroinflammation might then result in the acceleration of underlying neurodegenerative pathology. Alternatively, in individuals without underlying neurodegenerative pathology, delirium might be associated with neuronal injury, with 'de novo' mechanisms leading to dementia.

Fig 1. Fong & Inouye, 2022[1]

Preadmission Med Eval

Potentially inadequate medication	Appropriated alternative medication
Benzodiazepines for insomnia	Mirtazapine 7.5--15 mg
Nonbenzodiazepines (Zopiclone, zolpidem)	Mirtazapine 7.5--15 mg
Tricyclic antidepressants	Mirtazapine 7.5--15 mg Pregabalin
SSRI	Pregabalin
Antipsychotics for sedation (e.g. Promethazine)	Mirtazapine 20–40 mg
Typical/ atypical antipychotics without any indication or off-label use for dementia	Stop medication, no alternatives
Tramadol	Hydromorphone
Piritramide	Hydromorphone
Oxycodone	Hydromorphone
Morphine (except palliative care)	Hydromorphone
Fentanyl (except palliative care)	Hydromorphone
Buprenorphin (except palliative care)	Hydromorphone
Fluorchinolone	Cephalosporines, Fosfomycin for uncomplicated cystitis

Adapted from Table 1: Duning et al, 2021[1]

- 2021 review from Germany summarizes some (not entirely evidence based) suggestions for medication adjustments prior to admission for elective surgery

Questions?

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