Delirium: Pathophysiology, Prevention & Treatment

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Off-label uses of medications will be discussed during this talk

Contributions

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Learning Objectives

Discuss	Discuss delirium signs, symptoms, and diagnosis
Understand	Understand the pathophysiology and potential prevention of delirium
Understand	Understand the principles of treatment and management of delirium

What is Delirium?

Syndrome with many potential presentations

Constellation of symptoms suggestive of global brain dysfunction or acute brain failure

AKA *encephalopathy, acute confusional state, acute brain failure, ICU psychosis*

Many potential etiologies

Many potential manifestations

Often missed (55-86% of cases)

Common: 11-42% of hospitalized patients; 85-90% terminally ill patients

Maldonado 2018, Hui 2023

Definition of Delirium: DSM-5-TR

- A disturbance in attention accompanied by reduced awareness of the environment
- Develops over a short period of time (hours to days), represents a change from baseline, and tends to fluctuate in severity during the course of the day
- An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception)
- Disturbance is a direct physiological consequence of another medical condition(s)
- Not better explained by another syndrome

Five Core Domains of Delirium

- Attentional deficits
- Cognitive deficits
- Circadian rhythm dysregulation
- Emotional dysregulation
- Psychomotor dysregulation

Common Features

- Clouded consciousness
- Perceptual disturbances
- Incoherent speech
- Disturbed sleep-wake cycle
- Increased or decreased activity
- Disorientation and memory impairment
- Fluctuating course
- Related to a medical etiology

Static Risk Factors

Increasing age

Medical conditions

- Number and severity of active medical issues

Vulnerable substrate

- Dementia, CVA, Inflammation, Space-occupying lesion, TBI
- ApoE4 allele

Inflammatory States

- Long bone fractures, burns, complex surgeries
- Post-op status

Modifiable Risk Factors

Medications

- Benzodiazepines
- Opioids
- Anti-cholinergic medications
- Certain antibiotics (e.g., cefepime)

Immobility

Metabolic disturbances

Poor oxygenation states

Life-Threatening Causes

- **W**ernicke’s encephalopathy; **W**ithdrawal reactions
- **H**ypoxia; Hypoperfusion of the CNS
- **H**ypoglycemia
- **H**ypertensive encephalopathy
- **I**ntracerebral hemorrhage; **I**nfection
- **M**eningitis/encephalitis; **M**etabolic
- **P**oisoning

Motoric Subtypes

Hypoactive (most prevalent, 15-80%)

- Psychomotor retardation, apathy, slowed speech, decreased alertness
- Often confused with depression
- May indicate sicker state

Hyperactive (least prevalent, 6-46%)

- Agitation, insomnia, hypervigilance, irritability, wandering
- Perceptual disturbances may be more common
- Often confused with mania, schizophrenia or anxiety

Mixed (11-55%)

Making the Diagnosis at Bedside

Delirium is a bedside diagnosis

- No blood tests or imaging will confirm the diagnosis

Rely on history

- Look at pattern of onset and progression of symptoms
- Patients often poor historians, so rely on family, staff

EEG

- Can help confirm the diagnosis but not 100% sensitive or specific
- Classic EEG pattern is diffuse background slowing (delta-theta waves)
- EEG will be normal or fast in delirium due to GABA withdrawal

Nurse screening tools, like the CAM and CAM-ICU useful, but a full clinical exam remains the gold standard

Machine learning tools have been created to improve detection

Tests of Attention

Finger Tap to Letters

Test of sustained attention

Easy for patients to perform and more interactive

Can be challenging with masks

Forward Digit Span

Average forward digit span is 5-7

Backward digit span in attention and working memory

Average backward digit span is 3-5

Bedside Cognitive Testing

Orientation

Work orientation questions into interview

“Where is home for you? How far away is that?”

“What day did you come into the hospital? How long ago was that?”

“What are you watching on TV? What’s happening?”

Months of the Year Backwards

Test of sustained attention, concentration, working memory, some executive functioning

More complex than days of the week backwards

Pay attention to speed, errors, omissions

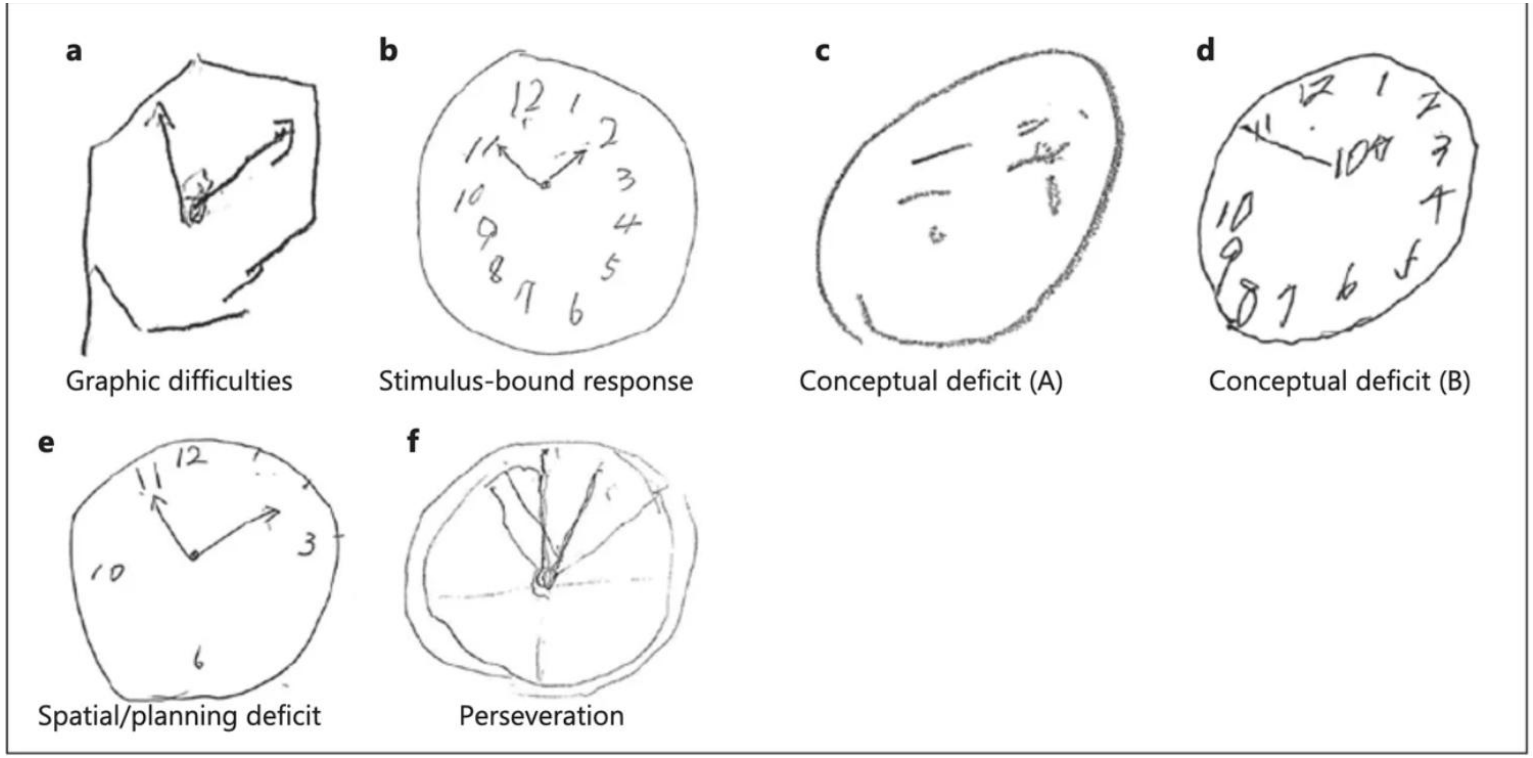
Clock Draw

Meant to be used as a serial exam

No distraction, no help

Domains tested:
Planning
Sequencing

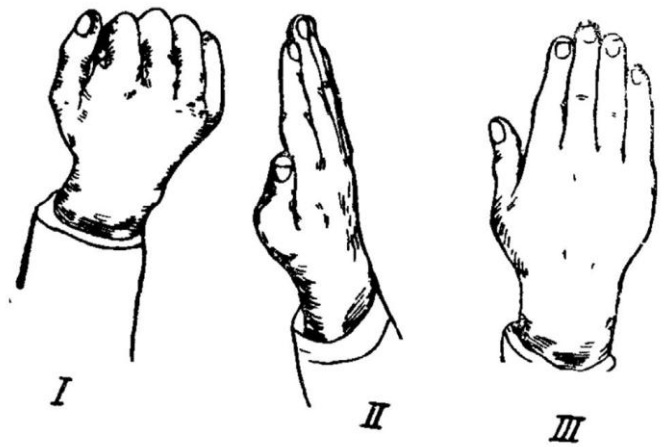
Primary Deficits Seen:
Poor planning
Perseveration
Stimulus Bound



From: https://www.healthline.com/health/schizophrenia/clock-drawing-test-schizophrenia

Luria Sequence

- Instructions: “I’m going to do a series of three movements with my hand. Watch what I do and then try to repeat it.”
- Deficits are analogous to those seen in the clock draw



Pathophysiology

- Simplified version: Imbalance of dopamine and acetylcholine
- Likely involves neuroinflammation, neuronal aging, oxidative stress, neuroendocrine dysregulation, circadian dysregulation

Pathophysiology

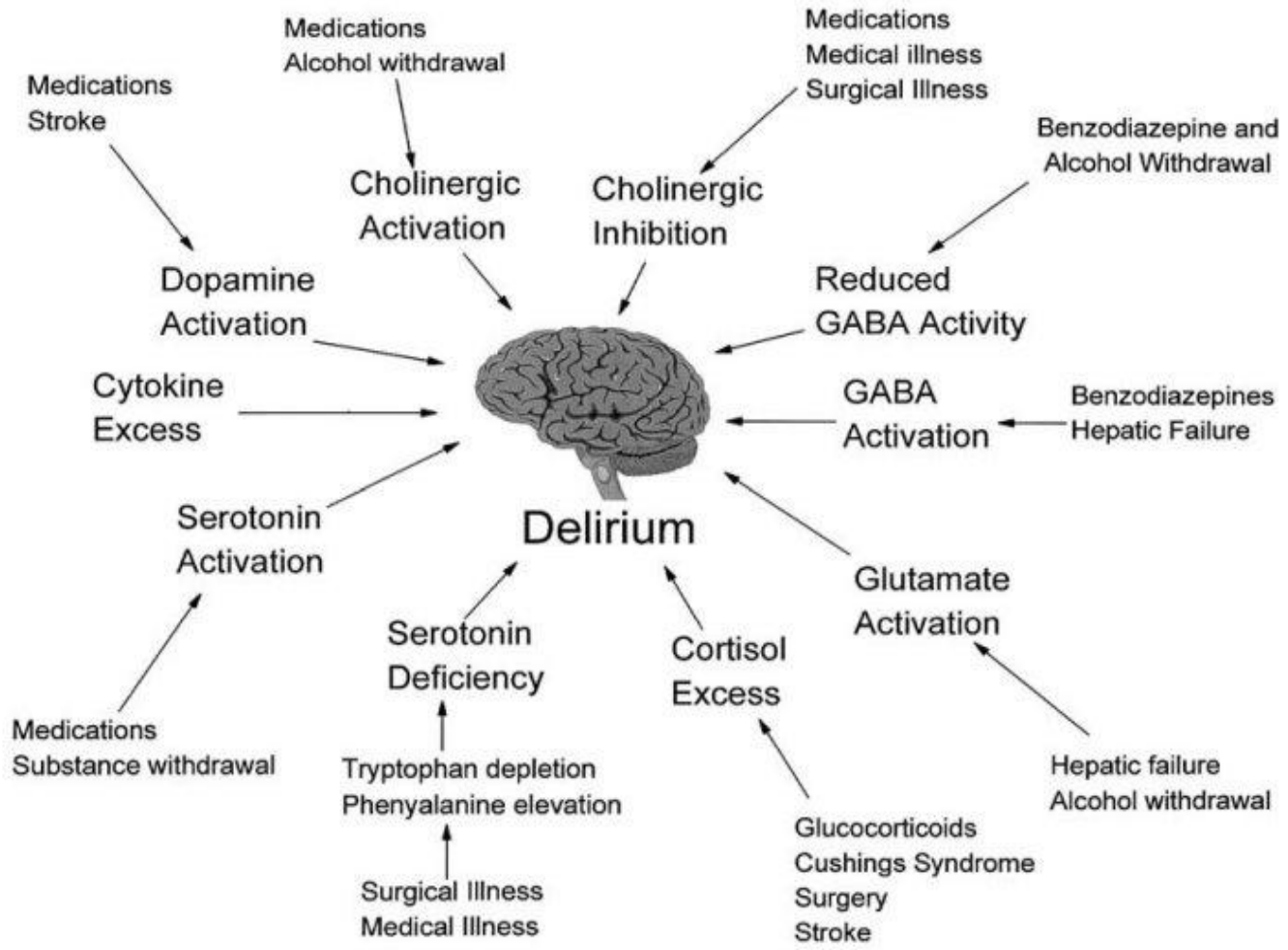


Figure 1. Pathophysiology of delirium. The evidence supports multiple mechanisms of delirium, which may pertain in different clinical situations. [Reproduced from Flacker and colleagues. *J Gerontol Biol Sci*. 1999;54A:B239–B246.]

Sequelae of Delirium

- Can be terrifying, disturbing, traumatizing
- Distressing to families who worry that it's permanent
- Agitation is #1 source of caregiver distress both in hospital and for home caregivers

Sequelae of Delirium

- Increased Mortality
  - 3-year mortality for hospitalized elderly with index episode of delirium was 75% vs. 51% for non-delirious controls
  - Delirious patients experienced an adjusted risk of death of almost 2.0 compared to non-delirious controls
- Increased Morbidity
  - Poor functional recovery
  - Possible future cognitive decline
  - Increased risk of complications
  - Increased nursing home placement
  - Increased costs and LOS

Curyto 2003, Mattison 2024

Sequelae of Delirium

Agitation

- Increases risk of harm to patient and staff
  - Pulling out IV's, central lines
  - Falls
  - Assaults on nursing and other staff

Perceptual Disturbances

- Increase risk for post-delirium PTSD (Post-ICU syndrome [PICS])

Persistent Delirium

- Subtype in the DSM-5-TR
- In hospital settings, delirium typically lasts days to 1 week, but may persist for weeks to months
- Not rare, especially in older individuals with dementia
  - Delirious symptoms persisted in 45% of elderly hospitalized patients at discharge
  - Symptoms were still present in 33% of elderly patients after 1 month, in 26% after 3 months, and in 21% after 6 months
- Has been associated with direct neuronal injury independent of dementia

Cole 2009; Tsui 2024

Does Delirium Cause Dementia?

- Prior work has suggested 5-10% of patients never recover cognitive baseline – develop dementia
- 2024 dose-response analysis suggests 3-fold higher rate of incident dementia in delirious patients (higher in men) and each additional delirious episode is associated with a 20% increased risk

Gordon 2024

Prevention, Treatment, Management

Can we prevent delirium with medications?

Can we treat delirium with medications?

Can we manage delirium with medications?

Prevention Strategies

Behavioral Approaches

- Effective with fewer adverse effects than medications

Calm, Quiet, Familiar

ABCDEF Bundle

- Awakening and breathing coordination, delirium prevention and management, early physical mobility, family engagement

Peng 2017; Yamanashi 2023; Matsuoka 2023; Hunt 2025; Cochrane 2016

Prevention Strategies

Choice of Analgesia and Sedation

- Compared with midazolam, patients who received dexmedetomidine for postoperative mechanical ventilation sedation had less risk of developing delirium
- 2021 study suggests no difference in risk between dexmedetomidine and propofol for mechanically-ventilated patients with sepsis
- Among opioids, dilaudid and oxycodone may be associated with lower rates of delirium than morphine

Some evidence that melatonin may help to prevent delirium

Orexin antagonists - evidence is mixed

NSAIDs have shown modest reduction in incidence in one retrospective cohort study

Peng 2017; Yamanashi 2023; Matsuoka 2023; Hunt 2025

Can We Prevent Delirium Using Antipsychotics?

Evidence base is mixed but not robust for antipsychotic agents

Prophylactic use of antipsychotics to prevent delirium is not currently supported by the literature

Kalisvaart 2005, Larsen 2010, Wang 2012, van den Boogaard 2013, Wu 2019

Can We Treat Delirium Using Medications?

- Conflicting evidence about whether medications can shorten the duration of delirium
- 2023 study showing haloperidol does not lead to increased days alive (but non-significant reduction in mortality seen)
- Preponderance of evidence: antipsychotic agents do not treat delirium
- The only treatment for delirium is to reverse the underlying cause and treat the medical illness
- *Devlin 2010, Breitbart 1996, Neufeld 2016, Girard 2018, Nikooie 2019, Wu 2019, Andersen-Ranberg 2023*

Non-pharmacologic Management Strategies

Screen	Screen for delirium every shift
Create	Create a calm, orienting environment (clocks, calendars, familiar objects from home)
Encourage	Encourage normal sleep-wake cycles
Involve	Involve family members in supportive care
Place	Place patient near nursing station
Ensure	Ensure glasses and hearing aids available
Monitor	Monitor fluid input and output
Discontinue	Discontinue all non-essential medications • "Clean the patient up"

Supportive Measures

- Nutrition, hydration
- Aspiration precautions
- Direct Observation to reduce restraints

Antipsychotics in Delirium

- Have been the mainstay of delirium management for decades
- Tranquilization
- In the 80’s and 90’s, intravenous haloperidol and chlorpromazine were used primarily
- Second generation antipsychotics now used more frequently
- Commonly-used agents include haloperidol, chlorpromazine, olanzapine, quetiapine
- Choice of antipsychotic often based on receptor profile, side effects, personal preference

Intravenous Haloperidol

- Haloperidol has high affinity for D2 receptors and little effect on sertonergic, alpha, histamine or cholinergic receptors
  - Also acts as a sigma-1 antagonist
- IV route preferred due to being fast-acting, and avoidance of pain, fear, and elevation of creatinine kinase caused by repeated IM injections
- Twice as potent as oral form, faster time to onset, long-lasting effect
- Calming but not sedating
  - Potentiates sedative effects of other agents
- 2023 study demonstrates equal safety to atypicals in older patients
- 2025 meta-analysis suggesting haloperidol reduces all-cause mortality, has high probability of benefit and low probability of harm

Sos and Cassem 1980; Chang 1992; Kim 2023; Cheng 2025

Intravenous Haloperidol and QT

- Current FDA recommendation is for telemetry at all doses
  - Based on 70 reports of QTc prolongation or TDP; all had multiple other risk factors
- Recent prospective studies indicate doses up to 20mg not associated with QT prolongation
- Revised Recommendations
  - No ECG monitoring required if total dose <5 mg daily and less than 2 other risk factors present
  - Check a baseline ECG in a non-emergent situation and at least one follow-up ECG, preferably 30-60 minutes following administration, for doses >5 mg daily **OR** 2 or more risk factors
  - Consider daily ECG for total cumulative dose >25 mg
  - Consider continuous monitoring and/or alternative agents for QT_c > 500 ms **OR** total dose >100 mg
  - Minimal evidence to suggest that switching to another antipsychotic is safer
  - If there is enough concern about QT prolongation to stop using IVH, use a non-antipsychotic agent
- 2024 study suggests limited value for ECG monitoring in ICU delirium patients, unless at increased risk

Beach 2020; Stollings 2024

Olanzapine

- "Atypical" or second-generation antipsychotic
  - Dopamine and serotonin (5HT2A) antagonist—also anticholinergic, antihistaminergic
- **ROUTES:** PO, SL, IV, IM

- **PROS**
  - Less associated with EPS/motor side effects than first generation antipsychotics
  - "Dirtier" drug - sometimes helpfully more overtly sedating
  - Helpful with nausea
- **CONS**
  - Dirtier drug can also mean: orthostasis, resp depression, urinary retention, etc.

Quetiapine

- "Atypical" or second-generation antipsychotic
  - Dopamine and serotonin (5HT2A) antagonist—also very anticholinergic, antihistaminergic
- **ROUTES:** PO
- **PROS**
  - Sedating
  - Less risk for EPS (especially at lower doses, e.g. 12.5-50mg)
  - Wide dose-range
- **CONS**
  - PO only
  - Dirtier drug can also mean: orthostasis, resp depression, urinary retention, etc.
  - Antipsychotic dose is >100 mg

Melatonin and melatonin-agonists

- Useful in restoring sleep-wake cycle
- May also have immune modulating effects
- Relatively benign safety profile

Chakraborti 2015

Alpha-2 Agonists

- Dexmetomadine associated with reduced rates of delirium compared with other sedatives
- Clonidine historically used for agitation in TBI and more recently applied as a management strategy in delirium
- Available in long-acting patch form
- Also used for alcohol and opioid withdrawal
- Can cause hypotension and bradycardia

Maldonaldo 2017

Valproic Acid

- Can be useful for impulsivity, agitation, dysexecutive syndrome in TBI and dementia patients
- Has been associated in at least one study with decreased antipsychotic usage
- Available IV and can be loaded for rapid titration
- Wide dose range
- Can cause pancreatitis, fulminant hepatic failure and hyperammonemia

Sher 2015

Trazodone

- Helpful for anxiety, irritability in addition to sleep
- May be particularly useful in older patients who cannot tolerate antipsychotics
- Only available PO
- Wide dose range
- Causes significant QTc prolongation
  - Nearly 20 ms at 150 mg
  - More than most antipsychotic agents

Tellone 2020

Benzodiazepines

- Historic lore is that “Benzos are bad” for delirium
- May be necessary in certain causes of delirium (ETOH withdrawal, seizures)
- Low-dose benzos added to antipsychotics can enhance the effects and allow for lower dosing of antipsychotic agents
- 2019 meta-analysis suggested haloperidol and lorazepam combo may be ideal for managing delirium
- Available in a variety of forms, fast-acting

Wu 2019

Stimulants

- Used at times for hypoactive delirium with significant apathy
- Mild effects on heart rate, blood pressure
- Risk of worsening psychosis
- Typical agent is methylphenidate 5mg qam, with gradual titration by 5-10mg daily

Approach to Delirium in Clinical Practice

- Look for underlying cause (may be more than one)
- Focus on treatment of the underlying condition
- Employ behavioral strategies
- Use interdisciplinary team approach
- Consider adjunctive medications when applicable
- Re-assess your treatment

Take Home Points

- Delirium is common and under-recognized
- Executive dysfunction is the most common cognitive deficit
- Hypoactive delirium is the most common motoric subtype
- Any illness process that affects the brain increases the risk of delirium
- Delirium is a bedside diagnosis, and basic bloodwork and imaging may be normal in many cases
- The treatment for delirium is to reverse the underlying cause
- Medications are used to manage the sequelae of delirium

References

Baller EB, Hogan CS, Fusunyan MA, et al. Neurocovid: Pharmacological Recommendations for Delirium Associated With COVID-19. Psychosomatics. 2020 May 21:S0033-3182(20)30153-5.

Beach SR, Gomez-Bernal F, Huffman JC, Fricchione GL. Alternative treatment strategies for catatonia: A systematic review. Gen Hosp Psychiatry. 2017 Sep;48:1-19.

Beach SR, Gross AF, Hartney KE, et al. *Intravenous haloperidol: A systematic review of side effects and recommendations for clinical use.* Gen Hosp Psychiatry. 2020 Aug 22;67:42-50.

Beschin N, MacPherson SE, Barozzi N, Della Sala S. Luria's fist-edge-palm test: A small change makes a big difference. Cortex. 2023 Dec;169:191-202.

Brietbart W, Marotta R, Platt MM, et al. A double-blind trial of haloperidol, chlorpromazine and lorazepam in the treatment of delirium in hospitalized AIDS patients. Am J Psychiatry 1996;153(2):231-7.

Chakraborti D, Tampi DJ, Tampi RR. Melatonin and melatonin agonist for delirium in the elderly patients. Am J Alzheimers Dis Other Demen. 2015 Mar;30(2):119-29.

Chang, W.H., et al., *Pharmacokinetics of haloperidol and reduced haloperidol in Chinese schizophrenic patients after intravenous and oral administration of haloperidol.* Psychopharmacology (Berl), 1992. 106(4): p. 517-22.

Cheng SL, Hsu TW, Kao YC, Yu CL, Thompson T, Carvalho AF, Stubbs B, Tseng PT, Hsu CW, Yang FC, Tu YK, Liang CS. Haloperidol in treating delirium, reducing mortality, and preventing delirium occurrence: Bayesian and frequentist meta-analyses. Crit Care. 2025 Mar 20;29(1):126.

Curyto KJ, Johnson J, TenHave T, et al: Survival of hospitalized elderly patients with delirium: a prospective study. Am J Geriatr Psychiatry 9:141-147, 2001.

Devlin JW, Roberts RJ, Fiong JJ, et al. Efficacy and safety of quetiapine in critically-ill patients with delirium: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study. Crit Care Med 2010;38(2):419-27.

Devlin JW, Skrobik Y, Gélinas C, et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Crit Care Med. 2018 Sep;46(9):e825-e873.

Fang CK, Chen HW, Liu SI, et al. Prevalence, detection and treatment of delirium uin terminal cancer inpatients: a prospective survey. Jpn J Clin Oncol 2008;38(1):56-63.

Girard TD, Exline SS, Carson CL, et al. Haloperidol and ziprasidone for treatment of delirium in critical illness. NEJM 2018.

Gordon EH, Ward DD, Xiong H, Berkovsky S, Hubbard RE. Delirium and incident dementia in hospital patients in New South Wales, Australia: retrospective cohort study. BMJ. 2024 Mar 27;384:e077634.

References

Howland RH. QTc prolongation and haloperidol: just how risky is this drug? *Psychosomatics*. 2014 Nov-Dec;55(6):741-2.

Hsieh TT, Yue J, Oh E, et al. Effectiveness of multicomponent nonpharmacologic delirium interventions: a meta-analysis. JAMA Intern Med. 2015;175(4): 512–520.

Hunt T, Payne T, Brophy JM, Irons J, Wang AY, Cartwright C, Moran B, Loadsman JA, Sanders RD. Perioperative dexmedetomidine for the prevention of postoperative delirium after cardiac surgery: a systematic review, Bayesian meta-analysis, and Bayesian re-analysis of the DECADE trial. Br J Anaesth. 2025 Apr 30:S0007-0912(25)00158-8.

Inouye SK, Rushing JT, Foreman MD, et al: Does delirium contribute to poor hospital outcome? J Gen Intern Med 13:234-242, 1998.

Inouye SK, Bogardus ST Jr, Charpentier PA, et al. A multicomponent intervention to prevent delirium in hospitalized older patients. NEJM 1999; 340: 669.

Kalisvaart KJ, de Jonghe JF, Bogaards MJ, et al. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study. J Am Geriatr Soc 2005;53(10:1658-66.

Larsen KA, Kelly SE, Stern TA, et al. Administration of olanzapine to prevent postoperative delirium in elderly joint-replacement patients: a randomized controlled trial. Psychosomatics 2010;51(5):409-18.

Kang J, Lee M, Ko H, et al. Effect of nonpharmacological interventions for the prevention of delirium in the intensive care unit: a systematic review and meta-analysis. J Critical Care 2018;48:372–384.

Kim DH, Lee SB, Park CM, et al. Comparative Safety Analysis of Oral Antipsychotics for In-Hospital Adverse Clinical Events in Older Adults After Major Surgery : A Nationwide Cohort Study. Ann Intern Med. 2023 Sep;176(9):1153-1162.

Leonard CE, Freeman CP, Newcomb CW, et al: Antipsychotics and the Risks of Sudden Cardiac Death and All-Cause Death: Cohort Studies in Medicaid and Dually-Eligible Medicaid-Medicare Beneficiaries of Five States. *J Clin Exp Cardiolog*. 2013;Suppl 10(6):1-9.

Leucht S, Cipriani A, Spineli L, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet*. 2013;382(9896):951-62.

Maldonado JR. Acute Brain Failure: Pathophysiology, Diagnosis, Management, and Sequelae of Delirium. Crit Care Clin. 2017 Jul;33(3):461-519

Matsuoka A, Sogawa R, Murakawa-Hirachi T, et al. Evaluation of the delirium preventive effect of dual orexin receptor antagonist (DORA) in critically ill adult patients requiring ventilation with tracheal intubation at an advanced emergency center: A single-center, retrospective, observational study. Gen Hosp Psychiatry. 2023 Jul-Aug;83:123-129.

Meyer-Massetti C, Vaerini S, Ratz Bravo AE, et al. The FDA extended warning for intravenous haloperidol and torsades de pointes: how should institutions respond? J Hosp Med 2010;5(4):E8-16.

References

Neufeld KJ, Yue J, Robinson TN, et al. Antipsychotic medication for prevention and treatment of delirium in hospitalized adults: a systematic review and meta-analysis. J Am Geriatr Soc 2016;64(4):705-14.

Nikooie R, Neufeld KJ, Oh ES, Wilson LM, Zhang A, Robinson KA, Needham DM. Antipsychotics for Treating Delirium in Hospitalized Adults: A Systematic Review. Ann Intern Med. 2019

Peng W, Shimin S, Hongli W, et al. Ddelirium risk of dexmedetomidine and midazolam in patients treated with postoperative mechanical ventilation: a meta-analysis.Open Med. 2017;12:252-256

Sos, J. and N. Cassem, *The intravenous use of haloperidol for acute delirium in intensive care settings.* Psychic and neurological dysfunctions after open heart surgery. Thieme, Stuttgart, 1980: p. 196-199

Sher Y, Miller Cramer AC, Ament A, et al. Valproic Acid for Treatment of Hyperactive or Mixed Delirium: Rationale and Literature Review. Psychosomatics. 2015 Nov-Dec;56(6):615-25.

Straker DA, Shapiro PA, Muskin PR. Aripiprazole in the treatment of delirium. Psychosomatics. 2006 Sep-Oct;47(5):385-91.

Tellone V, Rosignoli MT, Picollo R, Dragone P, Del Vecchio A, Comandini A, Radicioni M, Leuratti C, Calisti F. Effect of 3 Single Doses of Trazodone on QTc Interval in Healthy Subjects. J Clin Pharmacol. 2020 Nov;60(11):1483-1495.

Traynor V, Cordato N, Burns P, eet al. Is delirium being detected in emergency? Australas J Ageing 2016;35(1):54-7.

Tsui A, Johnstone B, Heslegrave A, Zetterberg H, Watne LO, Neerland BE, Krogseth M, Cunningham C, MacLullich A, Muniz Terrera G, Davis D, Caplan G. Persistent delirium is associated with cerebrospinal fluid markers of neuronal injury. Brain Commun. 2024 Sep 18;6(5):fcae319.

van den Boogaard M, Schoonhoven L, van Achterberg T, et al. Haloperidol prophylaxis in critically ill patients with a high risk for delirium. Crit Care 2013;17(1):R9.

van Eijk MM, van den Boogaard M, van Muram RJ, et al. Routine use of the confusion assessment method for the intensive care unit: a multicenter study. Am J Respir Crit Care Med 2011;184(3):340-4.

Wang W, Li HL, Wang DX, et al. Haloperidol prophylaxis decreases delirium incidence in elderly patients after noncardiac syurgery: a randkomized controlled trial. Crit Care Med 2012;40(3):731-9.

Wilson JE, Carlson R, Duggan MC, et al. Delirium and Catatonia in Critically Ill Patients: The Delirium and Catatonia Prospective Cohort Investigation. Crit Care Med. 2017 Nov;45(11):1837-1844.

Wu CS, Tsai YT, Tsai HJ: Antipsychotic drugs and the risk of ventricular arrhythmia and/or sudden cardiac death: a nation-wide case-crossover study. *J Am Heart Assoc*. 2015;4(2).

Wu YC, Tseng PT, Tu YK, Hsu CY, Liang CS, Yeh TC, Chen TY, Chu CS, Matsuoka YJ, Stubbs B, Carvalho AF, Wada S, Lin PY, Chen YW, Su KP. Association of Delirium Response and Safety of Pharmacological Interventions for the Management and Prevention of Delirium: A Network Meta-analysis. JAMA Psychiatry. 2019 May; 76(5): 526–535.

Yamanashi T, Sullivan EJ, Comp KR, Nishizawa Y, Akers CC, Chang G, Modukuri M, Tran T, Anderson ZEM, Marra PS, Crutchley KJ, Wahba NE, Iwata M, Karam MD, Noiseux NO, Cho HR, Shinozaki G. Anti-inflammatory medication use associated with reduced delirium risk and all-cause mortality: A retrospective cohort study. J Psychosom Res. 2023 May;168:111212.