

Delirium in the Medical Hospital

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Delirium

- **Definition**
- Epidemiology
- Risk Factors & Etiology
- Neuropathogenesis
- Financial Impact & Length of Stay
- Morbidity & Mortality
- Relationship to Dementia
- Work-up & Treatment
- Recovery

Delirium

- Also known as:
 - Altered Mental Status
 - ****Acute Brain Failure****
 - Encephalopathy
 - Acute Confusional State
 - ICU Psychosis
 - Hepatic/Hypoxic/Uremic/etc. Encephalopathy
 - Toxic Psychosis
 - Posttraumatic Confusion

Delirium in the DSM V

A. Disturbance in **Attention** (reduced ability to direct, focus, sustain and shift attention) **AND** Disturbance in **Awareness** (reduced orientation to environment)

B. Develops over hours to days, change from baseline and **fluctuates** during the day.

C. Additional disturbance in **cognition** (memory, disorientation, language, visuo-spatial ability or perception)

Delirium Definition

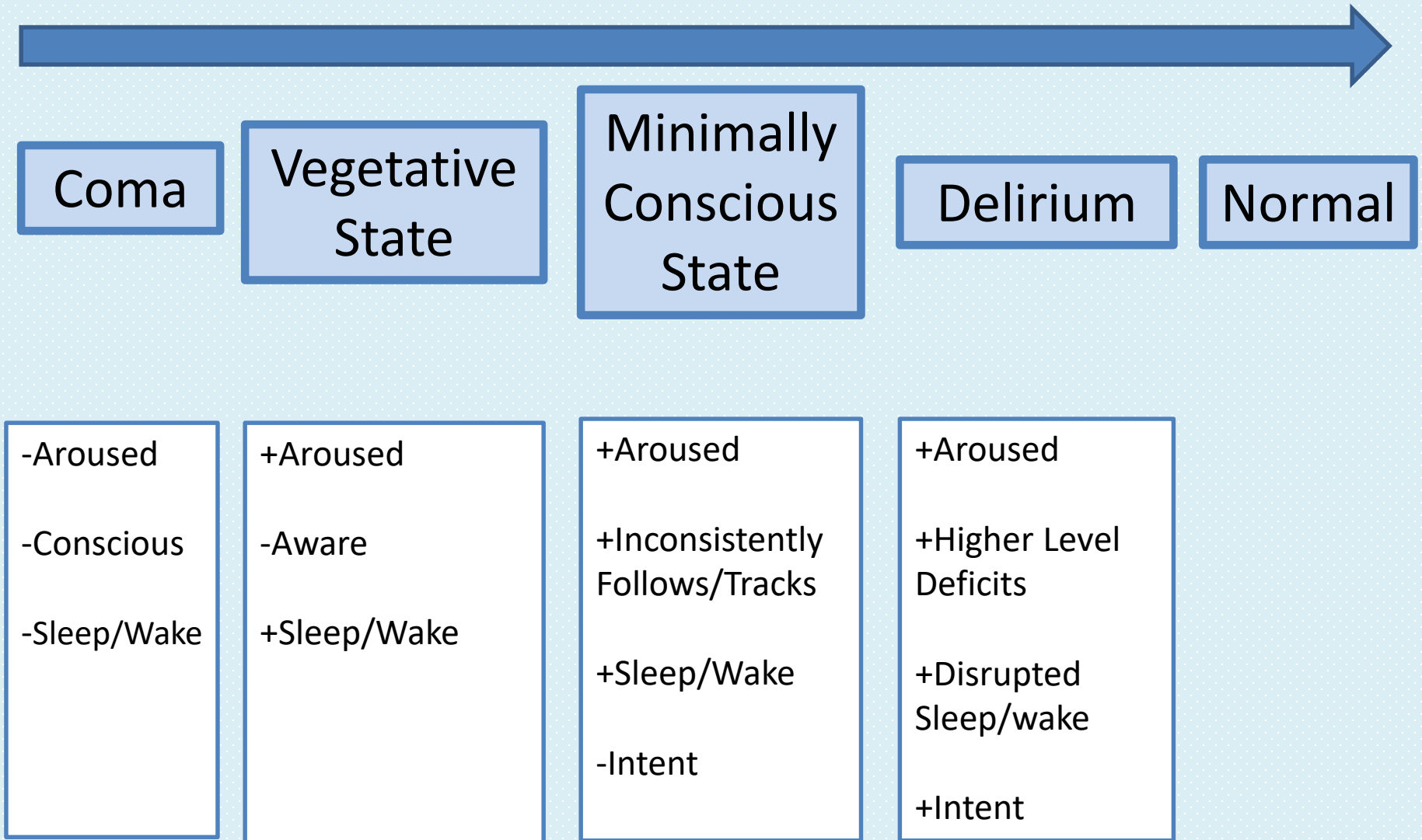
- ‘A serious disturbance in mental abilities that results in **confused thinking** and **reduced awareness** of your environment’. (*Mayo Clinic*)
- ‘An acute mental disturbance characterized by **confused thinking** and **disrupted attention** usually accompanied by disordered **speech** and **hallucinations**’. (*Webster*)
- Acute & fluctuating disorder of **Consciousness** (*attention, awareness of self/environment and wakefulness*), resulting in neuropsychiatric symptoms. (*Psychosomatic Medicine Textbook*)

Delirium

- Acute decline or change in mental status



Disorders of Consciousness



Findings in Delirium



Findings in Delirium

- Diffuse Cognitive Deficits
 - Inattention
 - Disorientation (time, place, person)
 - Impaired memory (short & long term, verbal & visual)
 - Visuo-constructional impairment
 - Executive function
 - Ability to abstract

Findings in Delirium

- Temporal Course
 - Acute or abrupt onset
 - Fluctuating severity over 24 hours
 - Usually reversible
 - Subclinical syndrome (precedes or follows)
 - Possible Prodrome?

Findings in Delirium

- Psychosis
 - Perceptual disturbance (illusions, AVTOG hallucinations)
 - Delusions (paranoid and poorly formed)
 - Thought disorder (tangential, circumstantial, LOA)

Findings in Delirium

- Sleep-Wake Disturbance
 - Fragmented throughout 24 hours
 - Reversal of normal cycle
 - Sleeplessness

Findings in Delirium

- Motor Behavior (often used to describe phenotype)
 - Hyperactive (30%)
 - Hypoactive (24%)
 - Mixed (46%)

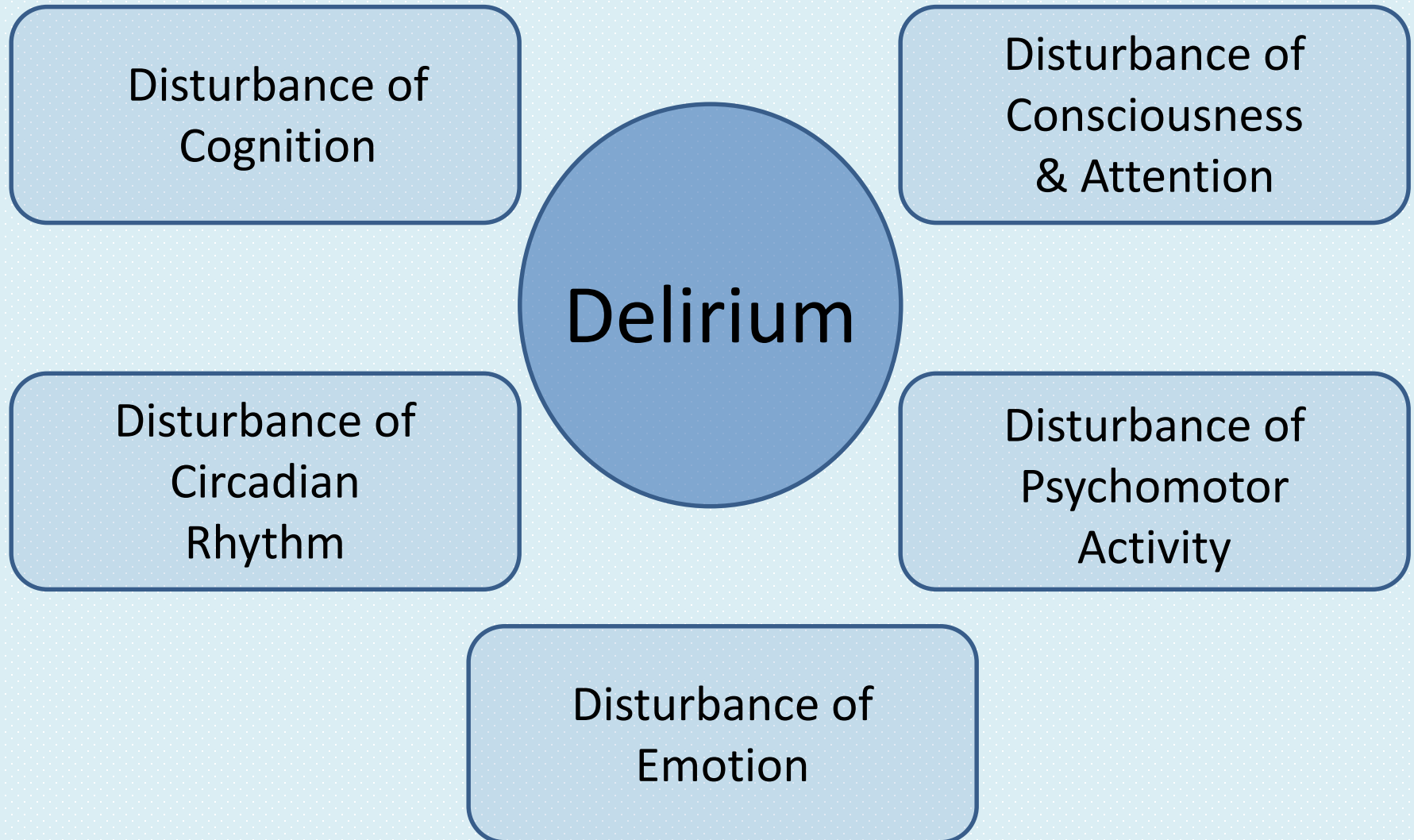
Findings in Delirium

- Language Impairment
 - Word-finding difficulty/paraphasia
 - Comprehension deficits
 - Altered semantic content
 - When severe, can mimic expressive/receptive aphasia

Findings in Delirium

- Altered or Labile Affect
 - Any mood can occur (commonly incongruent)
 - Anger or irritability
 - Hypoactive delirium 'labeled as depression'
 - Lability (rapid shifts)
 - Unrelated to mood preceding delirium
 - Fear
 - Anxiety
 - Perplexity

'The Clinical Picture'



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Epidemiology

• General Adults	- 10-24%	
• General Surgery	- 37-46%	
• Post-Op	- 10-60%	
• Stroke	- 13-48%	
• HIV/AIDS	- 20-40%	
• 'Frail-Elderly'	- 60%*	
• Medical ICU	- 60-80%	
• Advanced Cancer	- 85%*	
• CABG	- 25-32%	
• Cardiotomy	- 50-67%	
• B/L Knee Replacement	- 41%*	
• Femoral Neck Fx Repair	- 65%*	(*Denotes 'up to')

Epidemiology

- Emergency Room - 8-17%
- Nursing Home - 20-56%

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Risk Factors & Etiology

- *Age >75 years old*
- *Baseline cognitive dysfunction*
- *Male gender*
- Sensory impairment
- Use of IV lines, catheters, restraints
- Sleep deprivation
- Over-sedation
- Poorly controlled pain

Risk Factors & Etiology

- Infections (UTI and Pneumonia common)
- Hip fracture
- Hyper/Hypo- thermia
- Hypotension/Hypo-perfusion
- Hypertension ('encephalopathy')
- Hypoxia
- Malnutrition & nutrition deficiency
(Wernicke/B12, folate)

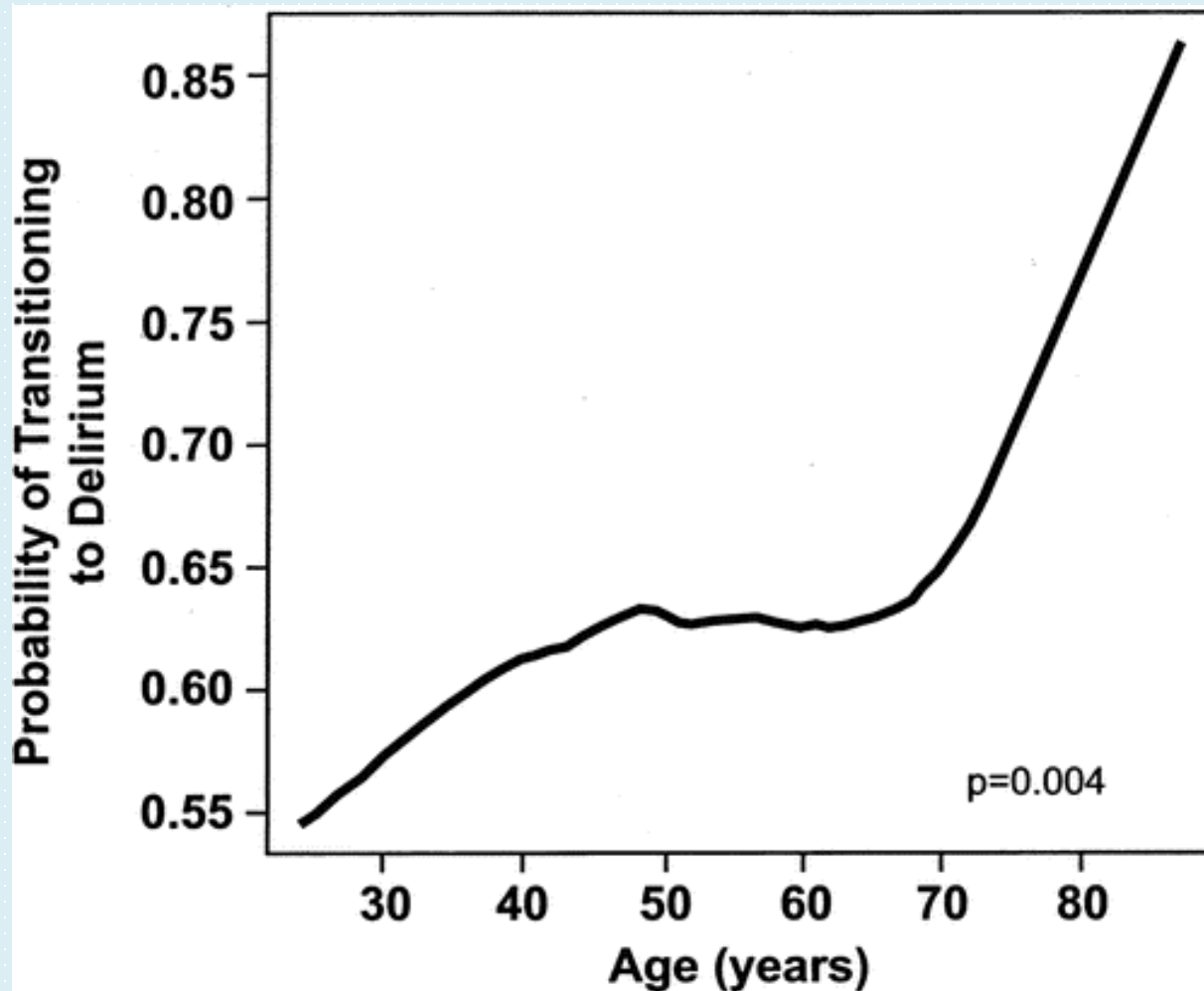
Risk Factors & Etiology

- Metabolic 'Encephalopathy' (cardiac, hepatic, renal, MI, PE)
- Endocrinopathy (thyroid)
- Electrolyte/water imbalance & dehydration
- Hyper/Hypo-glycemia, -natremia, -kalemia
- Dehydration
- Elevated cortisol
- Low Albumin

Risk Factors & Etiology

- CNS pathology (CVA, ICH, NPH)
- Trauma (physical or surgery)(burns)
- Medication (polypharmacy, psychoactive, serotonergic, anticholinergic, OTC)
- Substance abuse/withdrawal
- Heavy metals
- Toxins
- Cancer

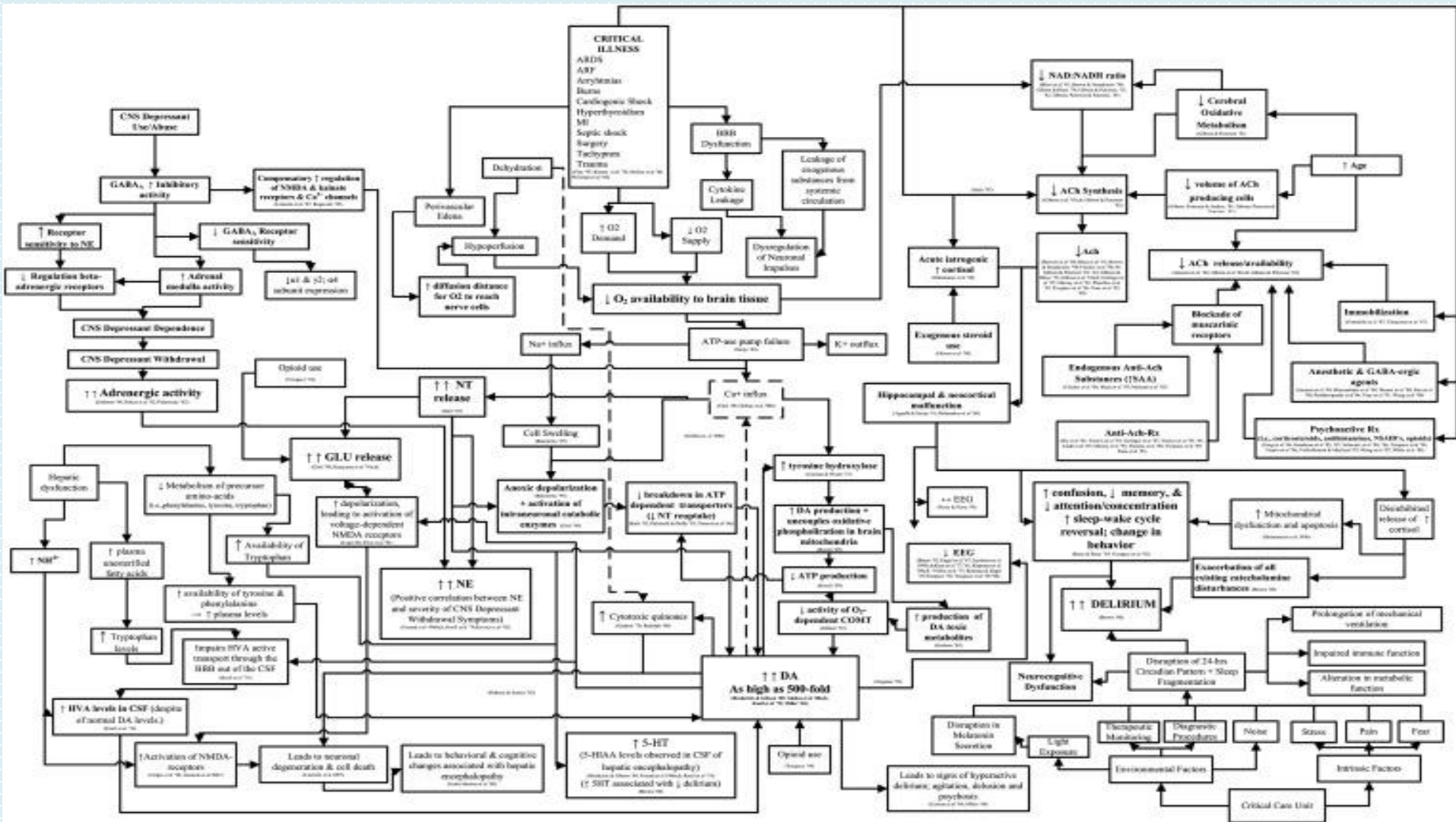
Probability Of Delirium vs Age



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Neuropathogenesis



Neuropathogenesis

- Impaired neurotransmitters and neural circuitry leads to a final pathway which results in a common clinical expression; delirium.
- The final neural network involves regions and circuits that support consciousness and higher level thinking.
- Dysfunction can occur in cortical and subcortical regions.
- EEG findings are generally seen ('diffuse slowing').

Neuropathogenesis

- Acetylcholine
 - Reduced cholinergic activity is the best established mechanism for delirium (Benadryl)
 - Cholinergic system is involved in:
 - Cortical activation
 - REM sleep induction
 - EEG fast-wave activity
 - Motor components of behavior
 - Attention, learning, memory, mood, etc.

Neuropathogenesis

- Dopamine
 - increased in delirium
- GABA
 - Increased or decreased in delirium
- Cytokines, false neurotransmitters, quinolinic acid, interleukin, C reactive protein, etc.

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Financial Impact of Delirium

- Costs Medicare \$164 billion per year. (2011)
- Costs hospital >\$11 billion per year.
- Post-hospital costs are \$153 billion per year
- Increased Re-hospitalization
- Increased ER visits
- Increased Institutionalization
- Increased Rehabilitation
- Increased Home care services
- Increased Caregiver burden

Financial Impact of Delirium

- Milbrandt et al. (2004) compared costs in mechanically ventilated MICU patients.
- Controlled for age, comorbidity of illness, degree of organ dysfunction, nosocomial infection, hospital mortality.
- *Median ICU cost* >\$13k for non-delirious patient and >\$22k for delirious patient.
- *Total hospital cost* >\$27k for non-delirious patient and >\$41k for delirious patient.

Length of Stay in Delirium

- Emond (2018)- Increased LOS by >4 days.
- Francis (1990)- Increased LOS by 5-10 days.
- McCusker (2003)- Increased LOS by >7 days.
- Han (2011)- Patients who were delirious in the ER stayed twice as long in the hospital when compared to non-delirious patients.

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Morbidity & Mortality of Delirium

- Functional & cognitive decline
- Increased rates of dementia
- Institutionalization
- Post-traumatic stress disorder
- Caregiver burden
- Poor participation PT & OT
- Pull tubes, IVs, catheters

Morbidity & Mortality of Delirium

- Self-harm from delusions and hallucinations
- Disruptive behavior
- Poor PO intake & failure to thrive
- Falls (head trauma & fractures)
- Decubitus ulcers
- Urinary incontinence & UTI
- Poor performance in ADL's
- Medication refusal

Morbidity & Mortality of Delirium

- Increased risk of death (4-65%)
- Increased risk of death (4-65%)
- **Increased risk of death (4-65%)**
- Francis (1990) notes 8% vs 1% rate of mortality in the elderly in the acute medical setting when delirium is present.
- Curyto (2001) 3 year mortality 75% vs 51%.

Recognition of Delirium

- 1 out of every 3 physicians recognizes delirium
- 1 out of every 3 nurses recognizes delirium
- In literature recognition of delirium is associated with less mortality and shorter length of stay (opposite is true as well)

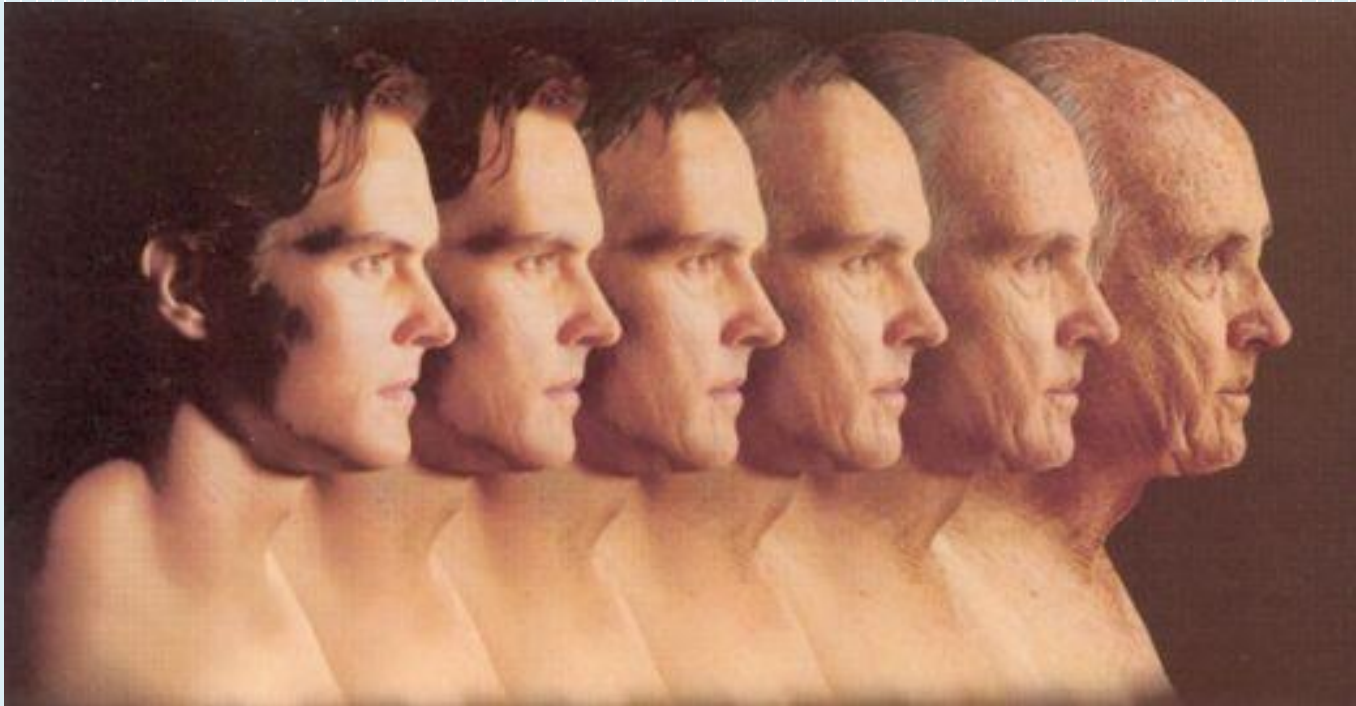
Delirium Rating Scales

RASS	Checklist	Delirium-O-Meter	Delirium Motor
IQCODE	Delirium Rating Scale-	Delirium Index	Checklist, Delirium
NEECHAM Confusion	revised version	Memorial Delirium	Motor Symptom Scale
Scale	Memorial Delirium	Assessment Scale	Richmond Agitation
Nursing Delirium	Assessment Scale	Confusional State	and Sedation Scale
Screening Scale	Confusion Assessment	Evaluation Scale	Motoric items of
Delirium Observation	Method	Delirium Assessment	Delirium Rating Scale,
Screening	CAM-ICU	Scale	Delirium Rating Scale-
Scale/Delirium	Pediatrics CAM-ICU	Delirium Severity Scale	Revised-98, Memorial
Observation Scale	Clinical Assessment of	Mini Mental Status	Delirium Assessment
Intensive care delirium	Confusion - A and B	Examination	Scale
screening checklist	Delirium Rating Scale	Cognitive Test for	Delirium Etiology
Pediatric Anesthesia	Delirium Rating Scale-	Delirium	Checklist
Emergence Delirium	Revised-98	Clock Drawing test	Pediatric Anesthesia
scale	Confusion Assessment	Digit Span Test	Emergence Delirium
Global Attentiveness	Method	Vigilance "A" Test	scale
Rating	Confusion Assessment	Mental state	Delirium Experience
Delirium Symptom	Method for Intensive	Questionnaire	Questionnaire
Interview	Care Unit assessment	Short Portable Mental	
Saskatoon Delirium	tool	Status Questionnaire	

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What is the Cognitive Baseline?



Figuring Out Baseline

- How long is your DAD having difficulty with memory? (*Duration/Trajectory*)
- When is the last time MOM was like you and I in terms of orientation, memory, interaction, etc.? (ask about *consistency of cognitive strengths*)
- When did you notice Grandpa get worse? (*acute worsening*)
- Did Grandma develop psychosis, mood, agitation, suicidality or homicidality? (*or is it old*)
- Find the impairment and track its course through history (*counting, spelling, bills, groceries, etc.*)

What is New & What is Old?

	Delirium	Dementia
Onset	Acute/Subacute	Insidious
Course	Fluctuating	Progressive
Reversibility	High	Low
Consciousness	Impaired	Clear until late stage
Attention/Memory	Inattention & Impaired short/ <u>long-term retrieval</u>	Attentive & Impaired short term retrieval (<u>long-term in late stages</u>)
Hallucinations	Commonly visual (or any other)	Visual or auditory
Delusions	Fleeting, fragmented, persecutory	Fixed and paranoid

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Work-up & Differential Diagnosis

- Discovering the etiology is key.
- Treating the underlying etiology is the 1st step in treatment.



Work-up & Differential Diagnosis

- Medication Evaluation
- CBC/BMP
- LFT
- TFT
- UA/Urine Culture
- Blood Culture
- Urine Toxicology/Blood Alcohol
- Thiamine/B12/Folate
- ESR
- NH3
- Chest X-ray
- Abdominal X-ray
- MRI Head/A/P
- EEG
- LP
- MRV
- D-Dimer
- ANA/DS-DNA
- ACE Level
- Glucose
- PTH
- Calcium
- EKG
- CK
- PO4
- HCG
- ALB
- HIV/RPR
- CT Head
- CT Abdomen/Pelvis
- Lyme
- Quantiferon
- Lead/Mercury/Other
- Antibody Spectrum
- PET scan

Non-Pharmacologic Treatment

- Correct malnutrition, electrolytes, dehydration.
- Remove immobilizing lines, tubes, catheters and restraints.
- Correct sensory deficits (glasses, hearing aids).
- Promote normal circadian rhythm (lights, curtains, noise).
- Environmental stimulation (orientation, TV, newspaper)
- Minimize isolation.

Pharmacologic Strategy

- Avoid anticholinergic medication.
- Avoid GABA-ergic drugs (BZD!!!!!!).
- Adequately treat pain.
- Avoid opioids for behavior.

On to symptom-targeted treatment with medication...

Neurochemical Pathways

Delirium Source	ACH	DA	GLU	GABA	5HT	NE	Trp	Phe	His	Cytok	HPA axis	NMDA activity	Changes in RBF	EEG	Mel	Inflam	Cort
Anoxia/hypoxia	↓	↑	↑	↑	↓	↓	↔	↑	↑, ↓	↑↑	↑	↑	↑	↓	↓	↑	↑
Aging	↓	↓	↓	↓	↓	↓	↓	↓	↓	↑↑	↑	↓	↑	↓	↓	↑	↑
TBI	↑	↑	↑	↑	↑	↑	↑	↑	↓	↑↑	↑	↑	↑	↓	↓	↑↑	↑
CVA	↓	↑	↑	↑	↑	↑	↑	↑	↓	↑↑	↑	↑	↑	↓	↓	↑↑	↑
Hepatic Failure (encephalopathy)	↔	↓	↑	↑	↑	↓	↑	↑	↑	↑↑	↑	↑	↑	↓	↓	↑	↑
Sleep deprivation	↓	↓	↑	↑	↑	↑	↓	↑	↑	↑	↑	↑	↑	↓	↓↑	↑↑	↑
Trauma, Sx, & Post-op	↓	↑	↑	↑	↓	↑	↓	↑	↑	↑	↑	↑	↑	↓	↓	↑	↑
ETOH & CNS-Dep Withdrawal	↑	↑	↑	↓	↑	↑	↓	↑	↑	↑	↑↑	↑	↓	↑	↓	↑	↑
Infection/Sepsis	↓	↓	↑	↑	↓	↓	↓	↓	↓	↑	↑↑	↑↑	↑	↓	↓	↑	↑
Dehydration & Electrolyte Imbalance	↔	↑	↑	↑	↓	↑	?	?	↑	↑	↑	↑	↓	↑	↓	↑↑	↑
Medical Illness	↓	↑	↑	↑	↓	↑	↓	↑	↑	↑	↓	↑	↑	↑	↓	↑	↑

Symptom-targeted Treatment

- General Treatment Options:
 - Melatonin (PO)
 - Precedex (IV)
 - Clonidine (PO, Patch or Epidural)
 - Zofran (PO/IM/IV)
 - Rivastigmine (PO or Patch)
 - Namenda/Donepezil/Amantadine (PO)
 - Tylenol (PO/IV)

Symptom-targeted Treatment

- Hyperactive/Agitation Phenotype:
 - Antipsychotics
 - Haloperidol/Haldol (PO/IM/IV)
 - Olanzapine/Zyprexa (PO/IM)
 - Risperidone/Risperdal (PO)
 - Quetiapine/Seroquel (PO)
 - Ziprasidone/Geodon (PO/IM)
 - AED/Mood Stabilizer
 - Valproic Acid/Depakote (PO/IV)
 - Oxcarbazepine/Trileptal (PO)
 - Carbamazepine/Tegretol (PO/IV)
 - Gabapentin/Neurontin (PO)

Symptom-targeted Treatment

- Hypoactive ('Depressed') Phenotype
 - Antipsychotics
 - Haloperidol/Haldol (PO/IM/IV)
 - Risperidone/Risperdal (PO)
 - Aripiprazole/Abilify (PO & IM unavailable)
 - Stimulants
 - Modafinil/Provigil
 - Amantadine
 - Bromocriptine
 - Memantine/Namenda

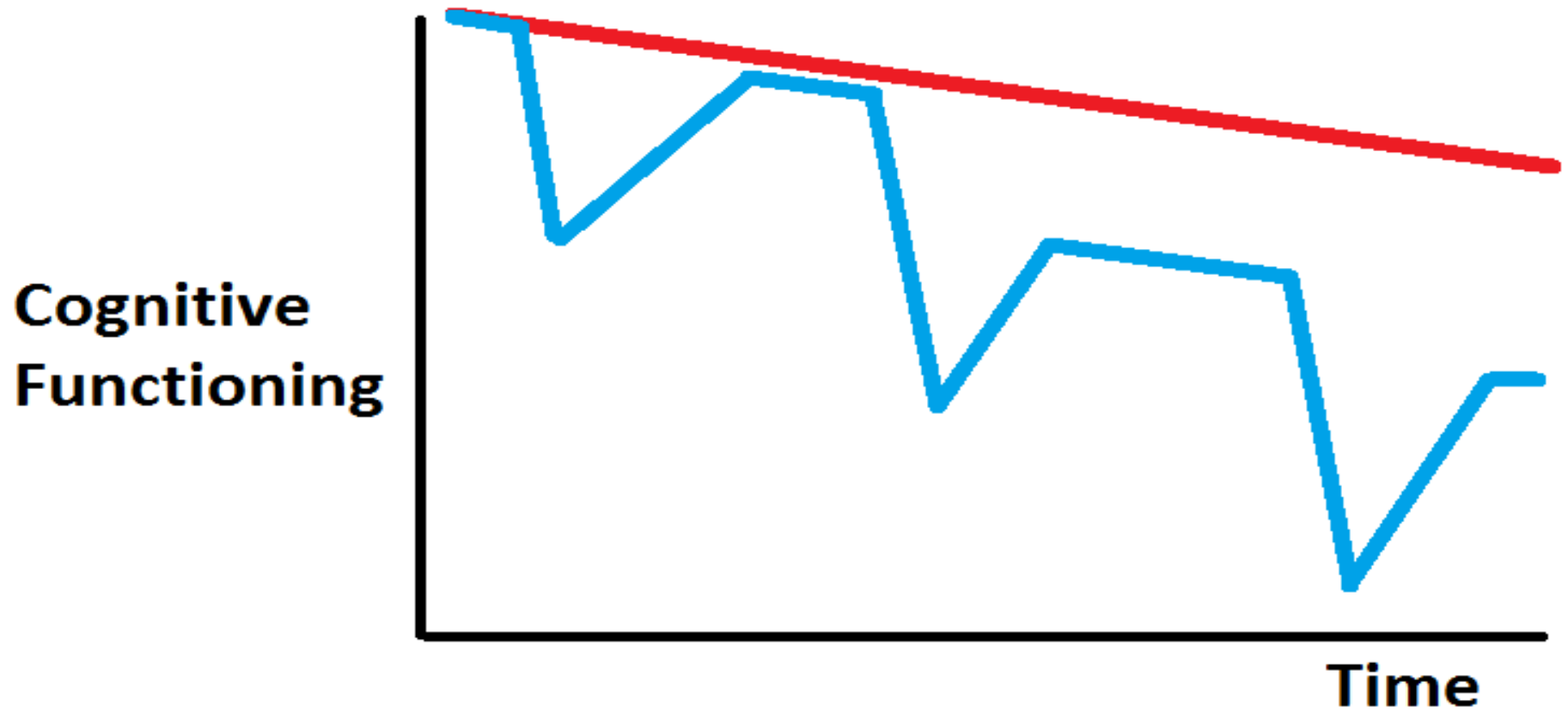
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Recovery

- Delirium by definition is reversible.
- Requires treatment of underlying cause and 'weeks to months' of time to formally 'recover'.
- Many follow-up studies showing poor cognitive performance months after acute delirium.

Recovery



Additional Considerations

- **Metoclopramide/Reglan** is a D2 antagonist, often given to children, pregnant women and elderly for nausea.
- **Prochlorperazine/Compazine** is a D2 antagonist given for nausea.
- **Promethazine/Phenergan** is a DA blocker and used for nausea. Created in 1940s.
- **Droperidol** is a D2 antagonist used for nausea and migraines.

Additional Considerations

- **Black Box Warning with Antipsychotics for Dementia with Psychosis**
 - Increased risk of death over 10 weeks (mode).
 - 2.6% in placebo group.
 - 4.5% in the treatment group.
 - Death due to cardiovascular causes.
 - *Ex: Heart failure & sudden death*
 - Death due to infectious causes.
 - *Ex: Pneumonia*
 - 1.6-1.7 times the risk of death in placebo patients

Additional Considerations

- Extra-pyramidal Symptoms
- Metabolic Syndrome
- EKG abnormalities
- Blood Dyscrasia
- Pancreatitis
-

A Final Thought...

- Is there a safer way to address acute agitation and/or psychosis in the elderly with delirium & dementia? Appetite? Sleep? Sadness?
- Please consider the route when answering this question; PO/IM/IV.

References

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Thank You

Questions