

# A State of Delirium, Is it Really Important to Worry About?



**RANDALL RICARDI, D.O.**  
**CHILD AND ADOLESCENT PSYCHIATRIST**

**BARROW**  
Neurological Institute



THE UNIVERSITY  
OF ARIZONA

COLLEGE  
OF MEDICINE  
PHOENIX

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# Disclosures



- Research Support-None to disclose



The patient is a 14-year-old female, admitted from the ER where she presented with acute onset psychosis. The family reports that 1 month ago, she was hospitalized in a psychiatric facility for auditory and visual hallucinations. The discharge diagnosis was Major Depression with Psychotic Features. Medications included Prozac 20mg po Qhs and Abilify 5mg po Qhs.

For 2 weeks, she was relatively stable, however, over the past 2 days she has been confused and agitated. They describe periods of time that she will stare blankly at the wall and cannot speak or move. At other times, she is pacing wildly, laughing to herself and attacking her family. She has not slept for 2 days and they have been unable to get her to eat or drink except to take her medications.

On the medical floor, she is screaming out, hitting staff, taking off her clothes and attempting to leave her room. She is not responding to your directions and is a danger to self and others.

Vitals: T 98.6, R 20, P 100, BP 135/85

# Learning Objectives



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# Objectives



- Describe the core diagnostic characteristics of delirium
- List the differential diagnoses for delirium
- Outline a treatment plan for the acute management of delirium

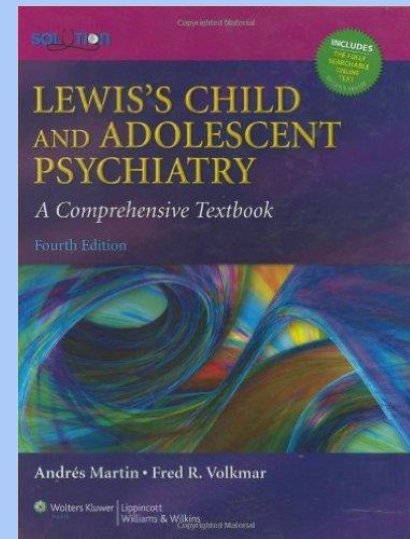


# Delirium



- First described by Leo Kanner in 1935 as “transient cerebral infections”
- Long period when the topic was not covered in textbooks
- Not described in DSM-V
- More recent publications on the topic due to the importance of the topic (1)

1. Schieveld et al, JAMA Pediatrics, 168:595-596



# Delirium



- Neuro-cognitive disorder due to a somatic illness or its treatment
- Brain may react to a critical illness with:
  - Fever
  - Epilepsy
  - Catatonia
  - Agitation
  - Coma
  - “Sickness behaviors” ( Loss of interest and appetite, irritability, tiredness and increased sleep )



# What is Delirium?

## DSM V Criteria:

- A. Disturbance in **attention** (i.e., reduced ability to direct, focus, sustain, and shift attention) and **awareness** (reduced orientation to the environment).
- B. The disturbance develops over a **short** period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to **fluctuate** in severity during the course of a day.
- C. An additional disturbance in **cognition** (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).
- D. The disturbances in Criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of **arousal**, such as coma.
- E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.



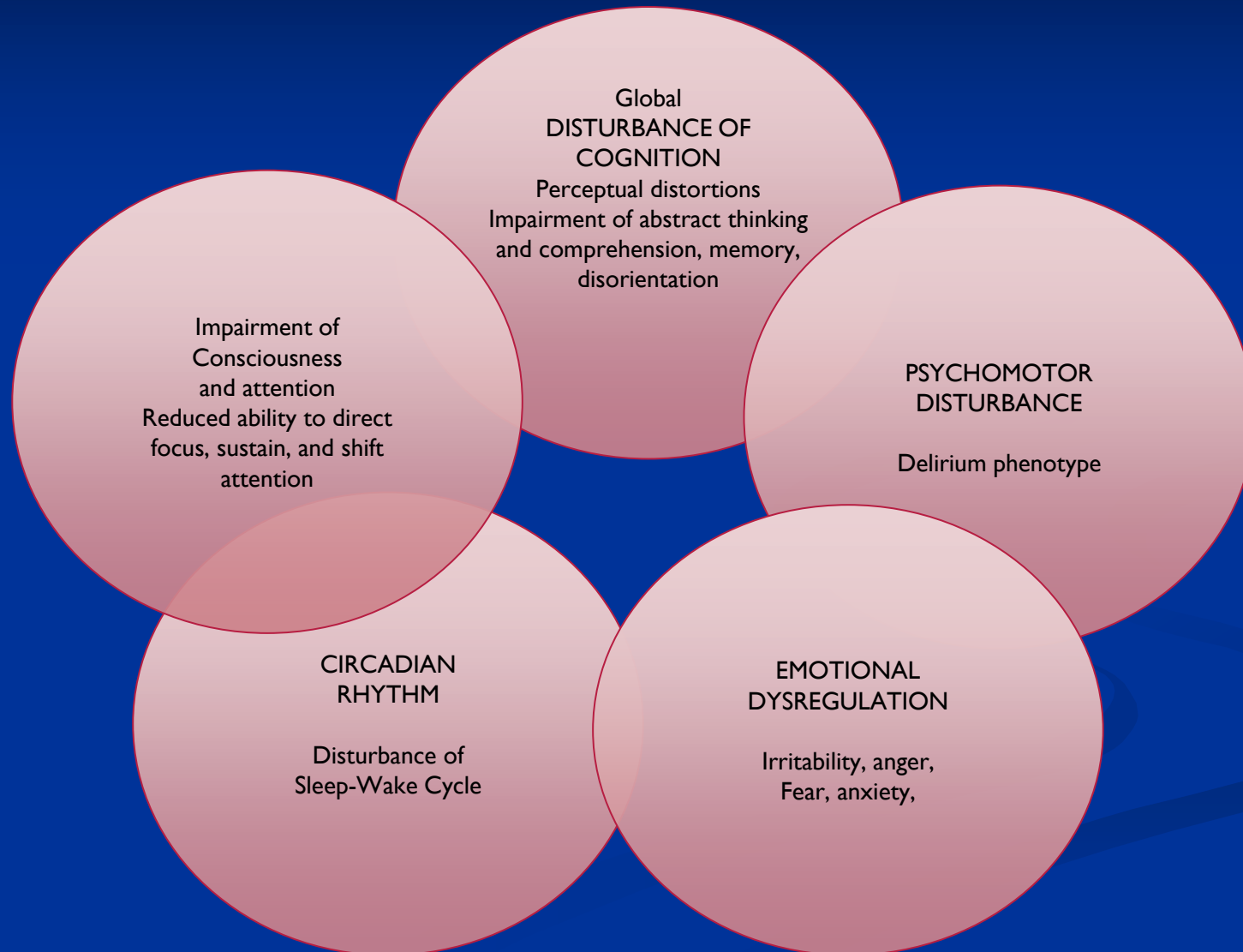
# Delirium



- Can present with fluctuating course
- Impairment in consciousness, attention and perception
- Change in cognition-memory, orientation
- Attention is the first to be lost and the last gained back



# Delirium Core Diagnostic Characteristics



# “The Great Imitator”



- Often misdiagnosed
  - Depression-withdrawn, flat affect
  - Mania-agitation, confusion
  - Psychosis-hallucinations, paranoia
  - Anxiety-restless
  - Dementia-cognitive impairment
  - Substance use-altered mental status

# Mortality in Delirium



- Incidence of delirium in critically ill children is 30%.
- Prognosis reflects the underlying cause of delirium.
- However delirium on it own is an independent risk factor for an increase in mortality.
- Mortality is about 20% which is similar to the rate in adults.
- Children and adolescents with delirium are at increased risk of problems in cognition and behavior for up to 3 months.
- Mortality is highest in those with organ failure and lowest in those with delirium following surgery or trauma.



# Delirium



- Occurs in 31% of ICU admissions
  - Increases to 81% when patients are intubated
- Most common cause of agitation in a general hospital
- May impact the treatment of the underlying illness (agitation, PTSD)
- Need to identify and treat the underlying cause



# Causes of Delirium



- Most common cause in children and adolescents is infection with CNS involvement.
- Delirium due to medications is common
- Studies have shown that delirium due to medications often require higher doses of atypical antipsychotics to treat.
- Any serious medical condition (trauma, autoimmune, post-transplant, post-operative, neoplasms, organ failure).



# I WATCH DEATH



- Infectious-encephalitis, meningitis, syphilis, pneumonia, UTI
- Withdrawal- alcohol, sedative-hypnotics
- Acute Metabolic-acidosis, alkalosis, electrolyte disturbance, hepatic/renal failure
- Trauma-Heat stroke, burns, postoperative
- CNS Pathology-abscess, hemorrhage, tumors, seizures, stroke, vasculitis, NPH
- Hypoxia-anemia, hypotension, PE, pulmonary/cardiac failure
- Deficiencies-B12, Niacin, Thiamine
- Endocrinopathies-alterations in blood sugar, thyroid, cortisol, parathyroid
- Acute Vascular-Hypertensive encephalopathy, stroke
- Toxins/drugs- medications, pesticides, solvents
- Heavy Metals-lead, manganese, mercury



# Misdiagnosis

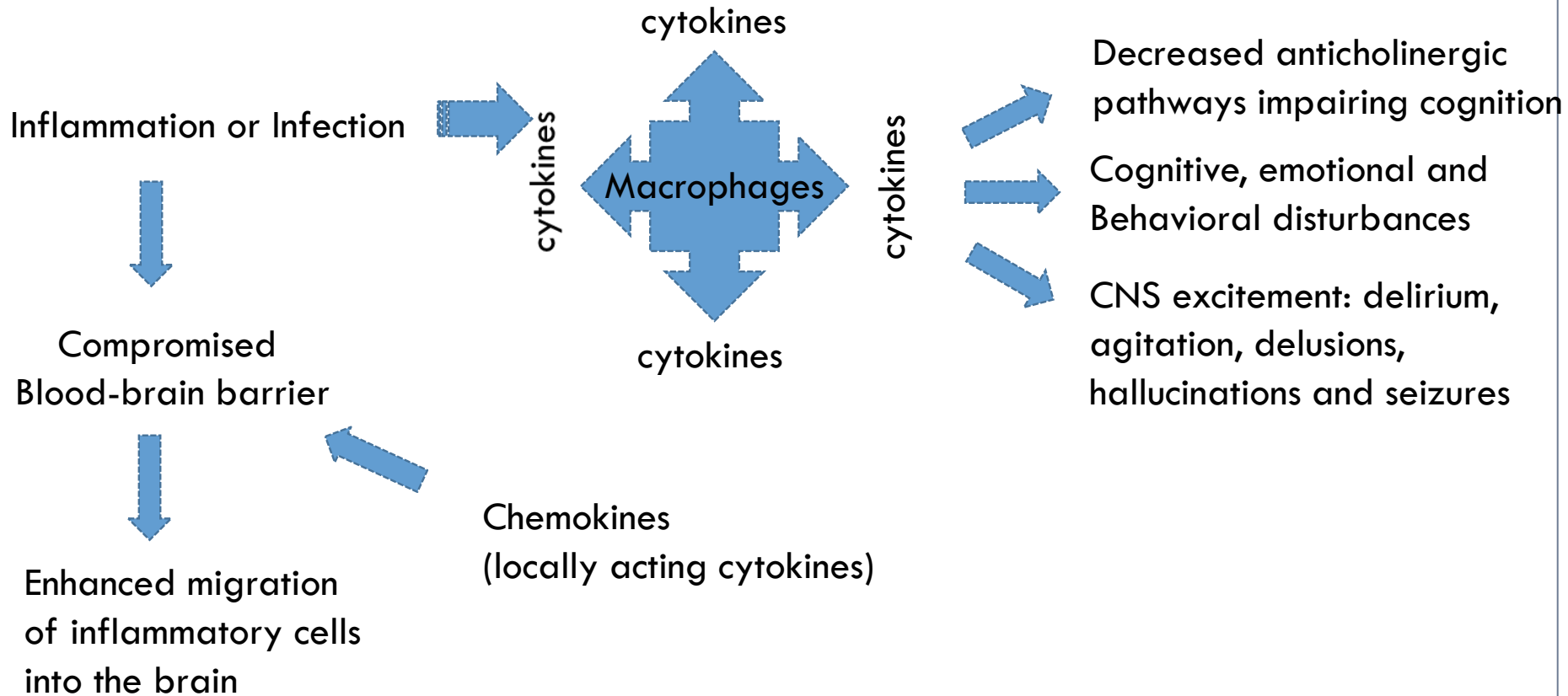


- A study at Johns Hopkins Children's Hospital looked at the rates at which pediatric teams recognized delirium and referred for a psychiatric evaluation. (1)
- 100% of the patients referred to psychiatry with a diagnosis of delirium were confirmed by psychiatry.
- 88.7% who were given a diagnosis of delirium by the psychiatric consult team had no mention of delirium in their charts. (depression, anxiety, PTSD, somatization and pseudo seizures)

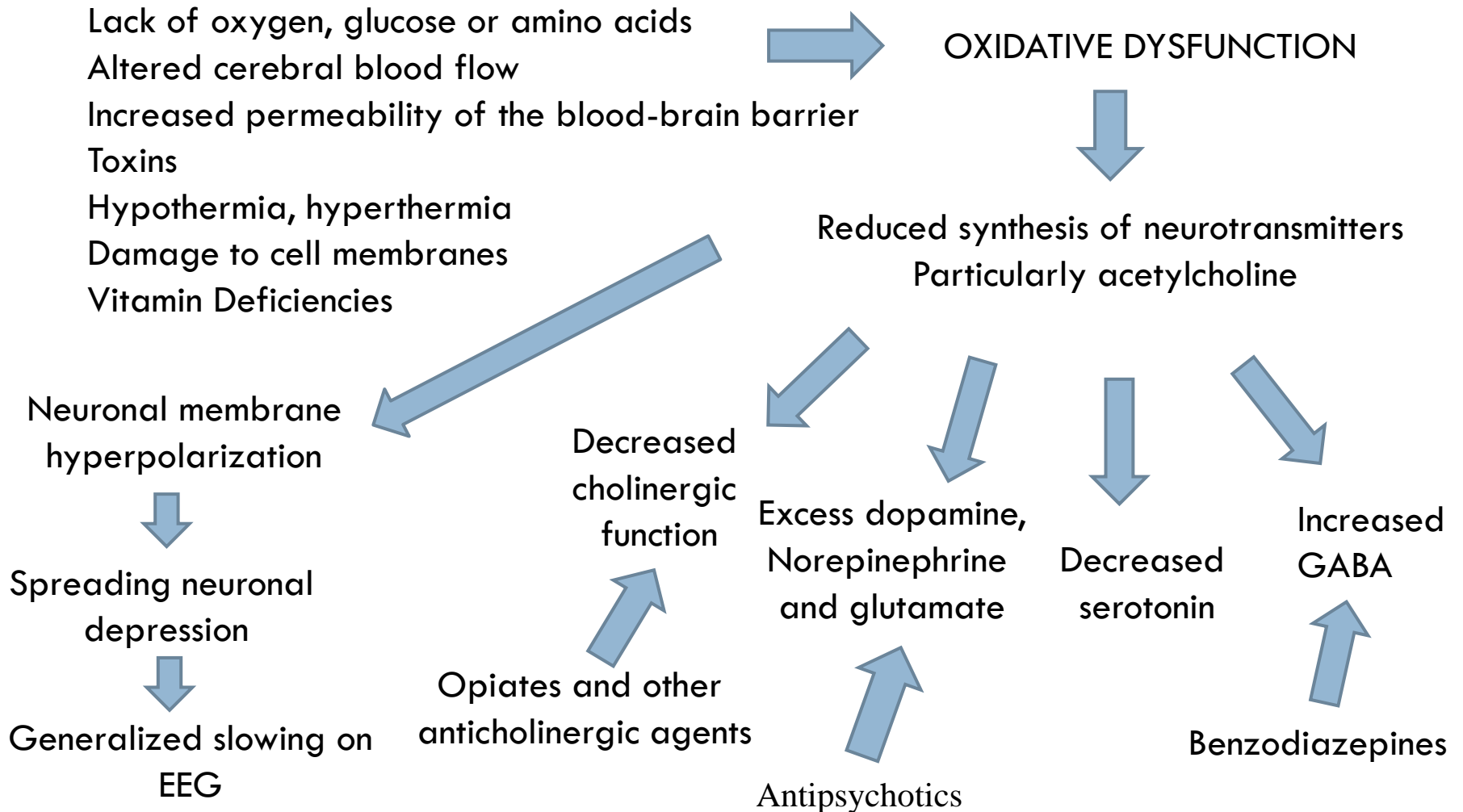
1. Patrick Kelly and Emily Frosch: 2012



# Why does delirium occur?



# Why does delirium occur?





# Why do we see psychosis in delirium?

- Macrophages secrete Cytokines in response to infections, surgery, injury
- Cytokines can cause a reduction of activity in the cholinergic Pathways
- Cytokines cause changes in sleep patterns, mood, behavior, cognition and memory
- Release of endogenous dopamine due to oxidative stress results in perceptual disturbances and paranoia that we label “psychosis”



# Delirium



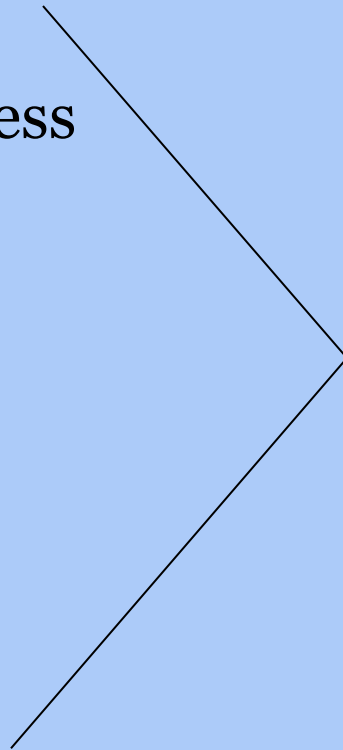
- Neurophysiologic basis
  - Hyperdopaminergic
  - Hypocholinergic activity in the RAS and the bilateral thalamic projections



# Assessment



- Appearance
- Level of consciousness
- Thought
- Speech
- Orientation
- Memory
- Mood
- Judgment
- Behavior



Age of Child  
Non-verbal  
Mechanically vented  
Coma  
ID



# “This is not my child”



- Does the child make eye contact?
- Are the child’s actions purposeful?
- Are they aware of their surroundings?
- Do they communicate their needs?
- Is the child restless?
- Is the child inconsolable?
- Is the child underactive?
- Does the child take a long time to respond?

# How is Delirium in Adults and Children Different?



- Study done in 2006 by Susan Turkel et al. compared the symptoms of delirium in adults and children across multiple studies.
  - More often found in children: sleep-wake disturbance, fluctuating symptoms, impaired attention, irritability, agitation, affective lability and confusion.
  - The same as adults: impaired alertness, apathy, anxiety, disorientation and hallucinations.
  - More often found in adults: impaired memory, depressed mood, speech disturbance, delusions and paranoia.



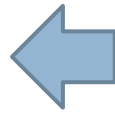
# What do we know about assessing Delirium in infants?



- Regulation of state and attention are fundamental roles of the CNS and alterations in these are critical to the diagnosis of delirium in infants.
- Attention in infants can be evaluated by looking at how they engage with caregivers, make eye contact and remain interested in the world around them.
- 4 Basic states: quiet awake, active fussy awake, drowsy or active sleep.
- Ability to maintain state depends on neurologic integrity and must assess eye movements, gross body movements, muscle tone and respiration.

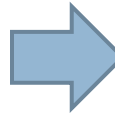




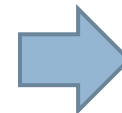


**Hyperactive:** The individual has a hyperactive level of psychomotor activity that may be accompanied by mood lability, agitation, and/or refusal to cooperate with medical care.

**Hypoactive:** The individual has a hypoactive level of psychomotor activity that may be accompanied by sluggishness and lethargy that approaches stupor.



**Mixed level of activity:** The individual has a normal level of psychomotor activity even though attention and awareness are disturbed. Also includes individuals whose activity level rapidly fluctuates.



# The Delirium Rating Scale (DRS)

- 10 item rating scale with a specific description that can be scored from zero to a maximum of 2,3 or4 depending on the item.
  - Designed to be used by psychiatrists and is labor intensive.
  - The sum of all the scores = the DRS score.
  - Highest possible score is a 32.
  - Does not rely on higher order cognitive function which is difficult to asses in young children.
  - Has been used to confirm diagnosis of delirium in children and adolescents.
  - Revised in 1998 (DRS-R-98) this version is used mainly in older children and adolescents
- \* 1. Temporal onset
  - \* 2. Perceptual disturbances
  - \* 3. Hallucinations
  - \* 4. Delusions
  - \* 5. Psychomotor behavior
  - \* 6. Cognitive status
  - \* 7. Physical disorder
  - \* 8. Sleep-wake cycle disturbance
  - \* 9. Lability of mood
  - \* 10. Variability of symptoms

**DRS-R-98 SCORESHEET**

Name of patient: \_\_\_\_\_ Date: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ Time: \_\_\_\_\_

Name of Rater: \_\_\_\_\_

SEVERITY SCORE:

TOTAL SCORE:

Severity Item	Item Score				Optional Information
Sleep-wake cycle	0	1	2	3	Naps Nocturnal disturbance only Day-night reversal
Perceptual disturbances	0	1	2	3	Sensory type of illusion or hallucination: auditory                      visual                      olfactory                      tactile Format of illusion or hallucination: simple                      complex
Delusions	0	1	2	3	Type of delusion: persecutory Nature:                      poorly formed                      systematized
Lability of affect	0	1	2	3	Type:                      angry                      anxious                      dysphoric elated                      irritable
Language	0	1	2	3	Check here if intubated, mute, etc.
Thought process	0	1	2	3	Check here if intubated, mute, etc.
Motor agitation	0	1	2	3	Check here if restrained <i>Type of restraints:</i>
Motor retardation	0	1	2	3	Check here if restrained <i>Type of restraints:</i>
Orientation	0	1	2	3	Date: Place: Person:
Attention	0	1	2	3	
Short-term memory	0	1	2	3	Record # of trials for registration of items: Check here if category cueing helped
Long-term memory	0	1	2	3	Check here if category cueing helped
Visuospatial ability	0	1	2	3	Check here if unable to use hands
Diagnostic Item	Item Score				Optional Information
Temporal onset of symptoms	0	1	2	3	Check here if symptoms appeared on a background of other psychopathology
Fluctuation of symptom severity	0	1	2		Check here if symptoms only appear during the night

# Cornell Assessment of Pediatric Delirium (CAPD)

- Overall Sensitivity: 94.1%, Specificity: 79.2%
  - ▣ In children with developmental delay Specificity 51.2%

RASS Score ____ (if -4 or -5 do not proceed)						
Please answer the following questions based on your interactions with the patient over the course of your shift:						
	Never	Rarely	Sometimes	Often	Always	Score
	4	3	2	1	0	
1. Does the child make eye contact with the caregiver?						
2. Are the child's actions purposeful?						
3. Is the child aware of his/her surroundings?						
4. Does the child communicate needs and wants?						
	Never	Rarely	Sometimes	Often	Always	
	0	1	2	3	4	
5. Is the child restless?						
6. Is the child inconsolable?						
7. Is the child underactive—very little movement while awake?						
8. Does it take the child a long time to respond to interactions?						
<b>TOTAL</b>						

- Ages 0-21
- Cutoff (9)

Cornell Assessment of Pediatric Delirium Item	Diagnostic and Statistical Manual Delirium Domains	Selected Normal Developmental Anchor Points*	
		Age (8 wk)	Age (1 yr)
1. Does the child make eye contact with the caregiver?	Consciousness	Follows moving object past midline, regards hand holding object, focused attention	Holds gaze. Prefers primary parent. Looks at speaker
2. Are the child's actions purposeful?	Cognition	Symmetric movements, will passively grasp handed object	Reaches and manipulates objects, tries to change position, if mobile may try to get up
3. Is the child aware of his/her surroundings?	Consciousness Orientation	Facial brightening or smile in response to nodding head, frown to bell, coos	Prefers primary parent, upset when separated from preferred caregivers. Comforted by familiar objects (i.e., blanket or stuffed animal)
4. Does the child communicate needs and wants?	Consciousness Psychomotor activity	Cries when hungry or uncomfortable	Uses single words or signs
5. Is the child restless?	Cognition Psychomotor activity Affect/distress	No sustained awake alert state	No sustained calm state
6. Is the child inconsolable?	Orientation Cognition Affect/distress	Not soothed by usual comforting actions, for example, rocking and singing	Not soothed by usual comforting actions, for example, singing, holding, talking, and reading
7. Is the child underactive—very little movement while awake?	Orientation Affect/distress	Little if any purposive grasping, control of head and arm movements, such as pushing things that are noxious away	Little if any play, efforts to sit up, pull up, and if mobile crawl or walk around
8. Does it take the child a long time to respond to interactions?	Consciousness Psychomotor activity	Not cooing, smiling, or focusing gaze in response to interactions	Not following simple directions. If verbal, not engaging in simple dialogue with words or jargon

\*Anchor points were developed for newborn and 4 wk, 6wk, 8wk, 28wk, 1 yr, and 2 yr olds.

# pCAM-ICU

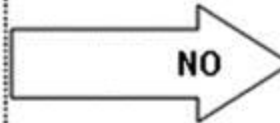


- Based on the CAM-ICU (The Confusion Assessment Method for the Intensive Care Unit) which is used in adults.
- Compared paired blinded assessments of Child Psychiatrists using DSM-IV criteria with assessments done by critical care team members (two pediatric intensivists, one pediatric critical care nurse practitioner, and three pediatric registered nurses) using the pCAM-ICU.
- Sensitivity 83%, Specificity 99%
- Requires patient cooperation, only for children >5 and limited in patients with developmental delay.



**1 Acute Change or Fluctuating Course of Mental Status**

- A. Is there an acute change from mental status baseline?  
OR  
B. Has the patient's mental status fluctuated during the past 24 hours?



**STOP  
NO DELIRIUM**

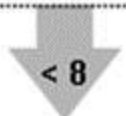


**2 Inattention**

- A. "Squeeze my hand when I say 'A'."  
Read the following sequence of letters: **A B A D B A D A A Y**  
**Errors: 1) No squeeze with 'A' and 2) Squeeze with letter other than 'A'.**  
B. If unable to complete ASE Letters → ASE Pictures



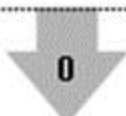
**STOP  
NO DELIRIUM**



**3 Altered Level of Consciousness**

Refer to current RASS (sedation assessment) score

RASS any score other than 0



**STOP  
DELIRIUM  
PRESENT**

**4 Disorganized Thinking**

- #1. Is sugar sweet? (Alternate: **Is a rock hard?**)  
#2. Is ice cream hot? (**Do rabbits fly?**)  
#3. Do birds fly? (**Is ice cream cold?**)  
#4. Is an ant bigger than an elephant? (**Is a giraffe smaller than a mouse?**)  
#5. **Command:** "Hold up this many fingers." (*Hold up 2 fingers.*)  
"Now do that with the other hand." (*Do not demonstrate.*)  
**OR** "Add one more finger." (*If patient unable to move both arms.*)



**NO DELIRIUM**



# psCAM-ICU



- 6months-5years old
- Or developmental age < 5 years old



# Screening



- **MMSE**
  - Writing
  - Clock Drawing
- **pCAM-ICU- Confusion Assessment Measure**
- **DRS- Delirium rating scale <3 years**
- **DRS-R-98 Older children and adolescents**



# Catatonia



- Motor immobility or stupor
- Excessive motor activity
- Extreme mutism or negativism
- Bizarre postures, stereotyped movements
- Echolalia or echopraxia



# Catatonia



- GABA - hypoactivity
- Dopamine - hypoactivity
- Glutamate NMDA-hyperactivity
- Serotonin - hyperactivity
- Cholinergic - hyperactivity





## Delirium

Increased DA  
Increased  
Glutamate  
Increased GABA  
Decreased AcH  
Decreased 5-HT

## Catatonia

Decreased DA  
Increased Glutamate  
Decreased GABA  
Increased AcH  
Increased 5-HT



# Treatment: Environmental Interventions

Frequent and repeated reassurance and reorientation by a caregiver

Limiting staff changes

Safe uncluttered environment

Calendars, clocks and objects from home

Minimizing ambient noise

Lights on during the day and off at night



# Antipsychotic Medications



- Not approved by FDA for treatment of delirium (off label)
- Few double-blind randomized control clinical trials
- Turkel et al. in 2012 did a retrospective chart review on 110 children and adolescents 1-18 years old using the DRS-R-98 looking at use of olanzapine, risperidone and quetiapine.
- Found significant decreases in DRS-R-98 scores ( $p < 0.001$ ) with minimal side effects.
- Some research suggests that Haldol is more effective for hyperactive delirium and risperidone is more effective for hypoactive/mixed delirium.



# Delirium in Infancy



- Recent study “Delirium in Infancy” Turkel et al., 2013 looked at 19 infants and toddlers ages 7-34 months.
- Looked at olanzapine and risperidone
- Olanzapine starting dose was 0.625 to 1.25mg qhs or bid.
- Risperidone was 0.05 to 0.1mg qhs or bid
- Target sx were control of insomnia and agitation
- Average duration of treatment was 38 days.
- DRS scores decreased significantly post treatment with antipsychotics ( $p < 0.0001$ )
- 3 patients died from underlying illness = mortality of 16%
- No side effects reported.



- Low and slow
- Monitor EKG
- Delirium rating scales TID
- Length of treatment unclear
- Taper off gradually





# Melatonin and Valproic Acid



- **Melatonin:** With the hypothesis that abnormal tryptophan metabolism is present in delirium there have been studies in the adult literature that melatonin may reduce the risk of developing delirium due to decreasing breakdown of tryptophan and serotonin.
- **Valproic Acid:** Recently published series of 6 case reports of using VPA to manage delirium and psychotic agitation in adults.



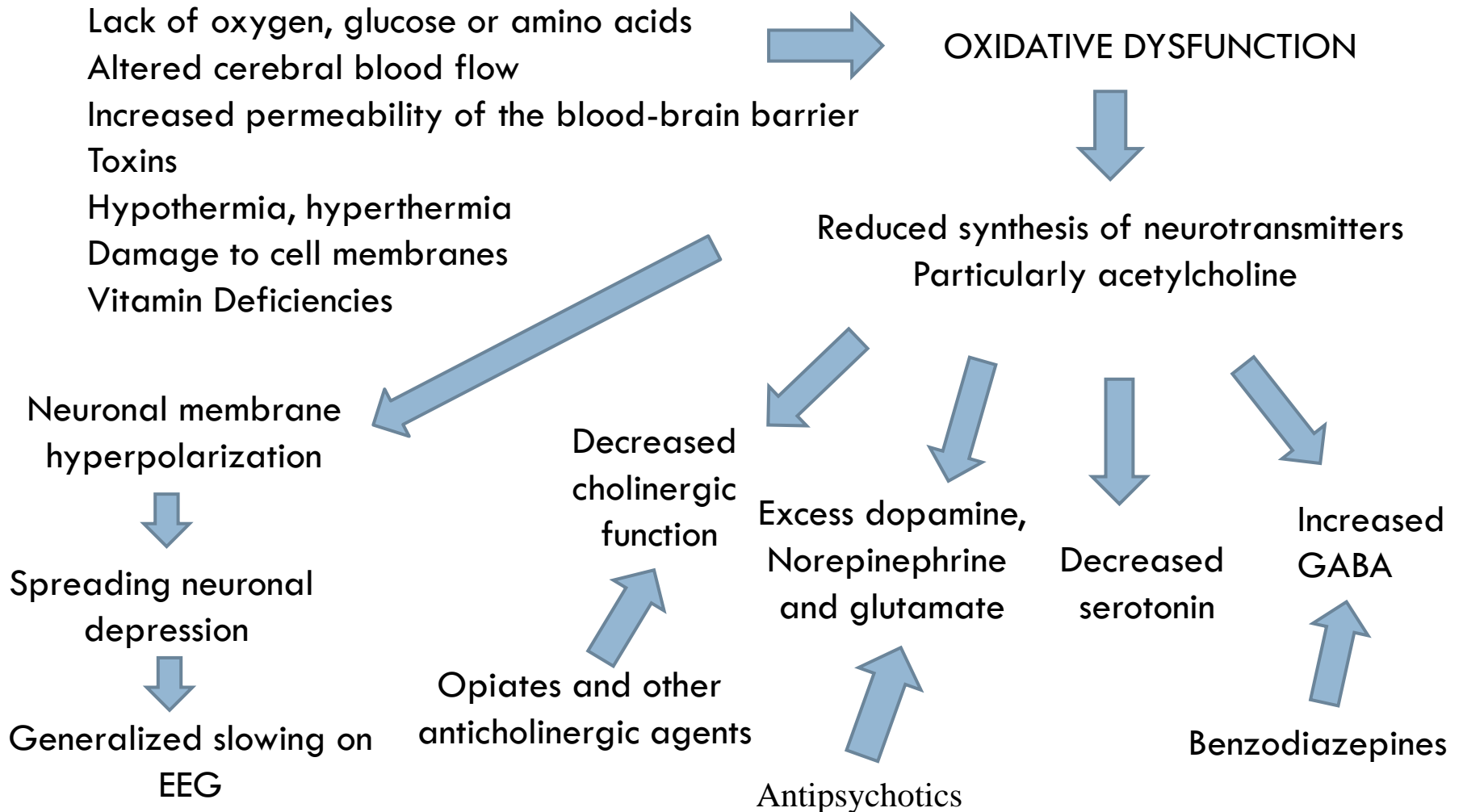
# Why do we say no benzodiazepines, anticholinergics or opiates?



- Anticholinergic agents (includes both antihistamines and opiates) further decrease acetylcholine which leads to impairment in memory and attention.
- Benzodiazepines increase GABA which is already elevated in delirium and leads to memory impairment and confusion which often leads to agitation.



# Why does delirium occur?



# Treatment Catatonia



- Benzodiazepines
- Glutamate antagonists-namenda
- Avoid antipsychotics
- ECT



The patient is a 14-year-old female, admitted from the ER where she presented with acute onset psychosis. The family reports that 1 month ago, she was hospitalized in a psychiatric facility for auditory and visual hallucinations. The discharge diagnosis was Major Depression with Psychotic Features. Medications included Prozac 20mg po Qhs and Abilify 5mg po Qhs.

For 2 weeks, she was relatively stable, however, over the past 2 days she has been confused and agitated. They describe periods of time that she will stare blankly at the wall and cannot speak or move. At other times, she is pacing wildly, laughing to herself and attacking her family. She has not slept for 2 days and they have been unable to get her to eat or drink except to take her medications.

On the medical floor, she is screaming out, hitting staff, taking off her clothes and attempting to leave her room. She is not responding to your directions and is a danger to self and others.

Vitals: T 98.6, R 20, P 100, BP 135/85

- What would be your initial workup?
- What is her differential Dx?
- What would be your treatment plan?

In the acute management of delirium, benzodiazepines are avoided for which of the following reasons:



- 1. Delirium results in increased CNS GABA
- 2. Delirium results in increased Dopamine (DA)
- 3. Delirium results in decreased cholinergic function
- 4. Delirium results in increased Glutamate

Question Rationale While Delirium results in all of the above changes in neurotransmitters, benzodiazepines are avoided because they further increase GABA levels, often contributing to a worsening of a delirium state. Knowing the basic changes to the neurotransmitter system, the drug of choice would be an antipsychotic that would decrease DA.

# Summary



- Delirium occurs more frequently than previously believed
- Important to identify delirium early due to the high mortality
- Differential diagnoses are broad
- Differentiating delirium from catatonia is critical for effective treatment outcomes
  
- [rricard@phoenixchildrens.com](mailto:rricard@phoenixchildrens.com)





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