PSYCHOSOCIAL SYMPTOMS (DELIRIUM)

FONDAZIONE MARUZZA LEFEBVRE D'OVIDIO ONLUS

2nd CONGRESS ON PAEDIATRIC PALLIATIVE CARE - A GLOBAL GATHERING
Rome 19th - 21st November 2014

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No conflict of interest to disclose

The purpose of this presentation…

Provide an overview of delirium , its pathophysiology, subtypes, assessment and evidence-based interventions, both pharmacologic and nonpharmacologic.

Pediatric Palliative care improves the quality of life of children who are facing chronic complex advanced or life-threatening conditions

These conditions are often associated with a significantly increased risk of psychosocial symptoms such as depression, anxiety and delirium...

What is Delirium?

Vol. 44 No. 4 October 2012 Journal of Pain and Symptom Management 583

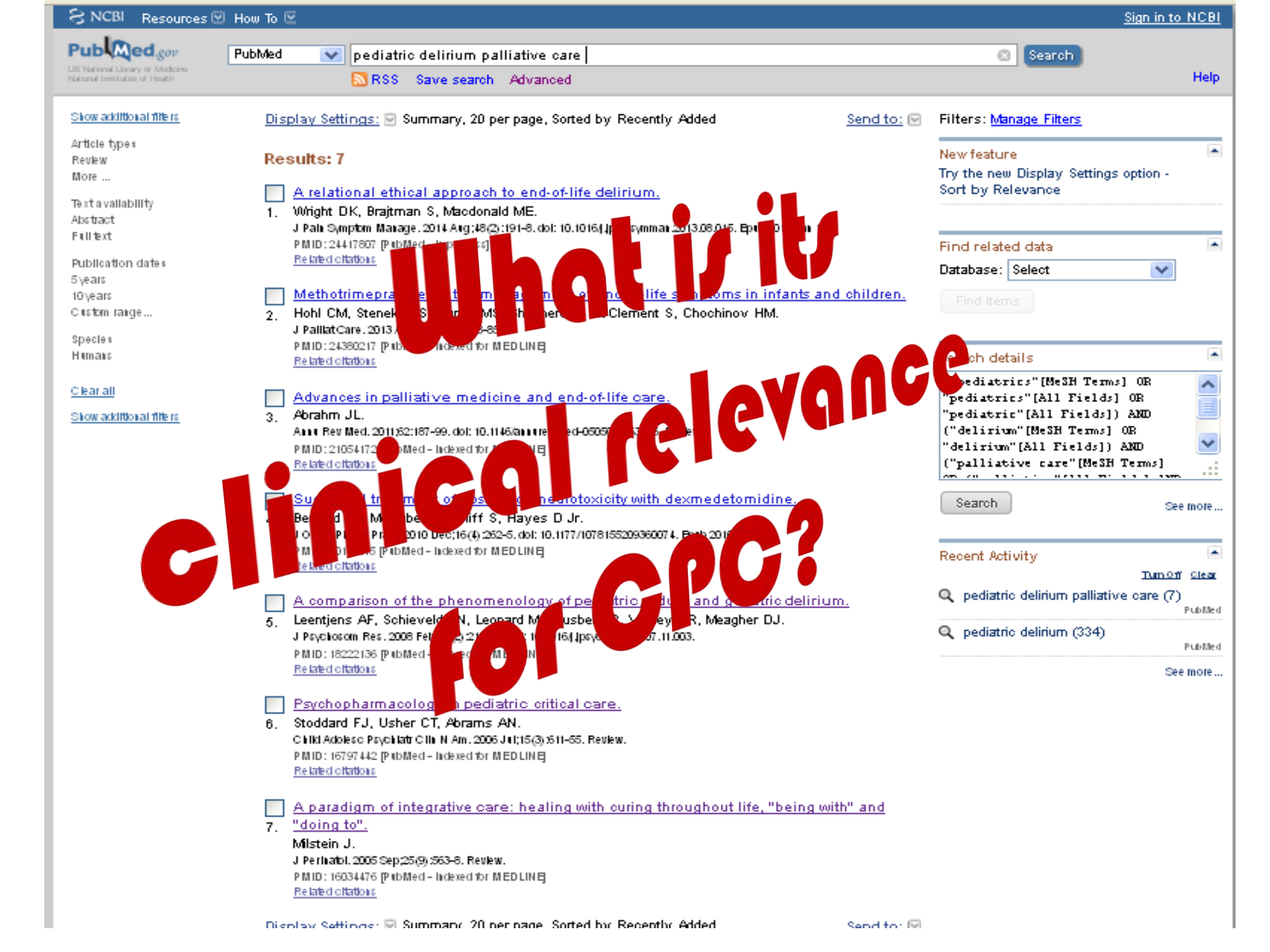
Review Article

Delirium in Palliative Medicine: A Review

Susan B. LeGrand, MD
Section of Palliative Medicine and Supportive Oncology, The Harry R. Horvitz Center for Palliative Medicine, Department of Solid Tumor Oncology, Cleveland Clinic Taussig Cancer Institute, Cleveland, Ohio, USA

Abstract
Delirium is a devastating complication of general medical and surgical populations but of particular importance in palliative medicine. It is a clinical syndrome that is often not recognized and, therefore, not treated appropriately. The presence of delirium is a predictor of increased morbidity and mortality, longer hospitalization, and more likely discharge to a nursing facility. This article reviews the pathophysiology, etiology, diagnosis, and treatment of delirium in the palliative medicine population. J Pain Symptom Manage 2012;44:583–594.

Key Words
Delirium, palliative medicine, antipsychotic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What is its clinical relevance for CPC?

Delirium: matters arising

- This condition is under-recognized and likely common in pediatric critical care
- Many children with hypoactive or mixed delirium may go unrecognized
- Often could be a reversible complication
- Evidence-based assessments of outcomes and interventions for pediatric delirium are lacking due to the absence of a simple and age appropriate reliable screening tool
- In relation to CPC it interferes with adequate clinical evaluation and impedes the patient from participating in decision making
- Diagnosis of delirium is only the start of the diagnostic process

Delirium: Prevalence

- **Estimated incidence of 10% of all inpatient referrals to child and adolescent consultation–liaison psychiatry services**

  Turkel S, Tavare C.
  Neuropsychiatry Clin Neurosci 2003

- **Between 17% and 66% of psychiatry referrals from pediatric intensive care**

  Schieveld J et al.
  Intensive Care Med 2007

- **Of all advanced cancer patients over 80% experience delirium in their final days**

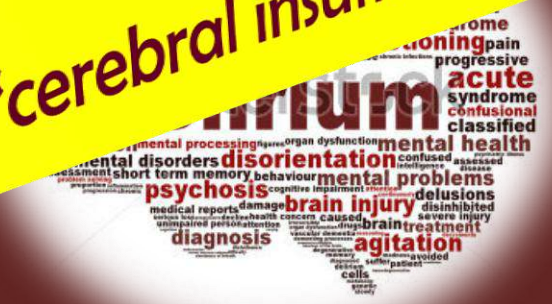
  Centeno C et al.
  Palliative Medicine 2004

Delirium is primarily a brain disfunction

Confusing Terminology:

Variety of terms used by different disciplines

'delirium', 'acute confusional state', 'acute organic brain syndrome', 'encephalopathy', 'ICU psychosis', 'cerebral insufficiency'



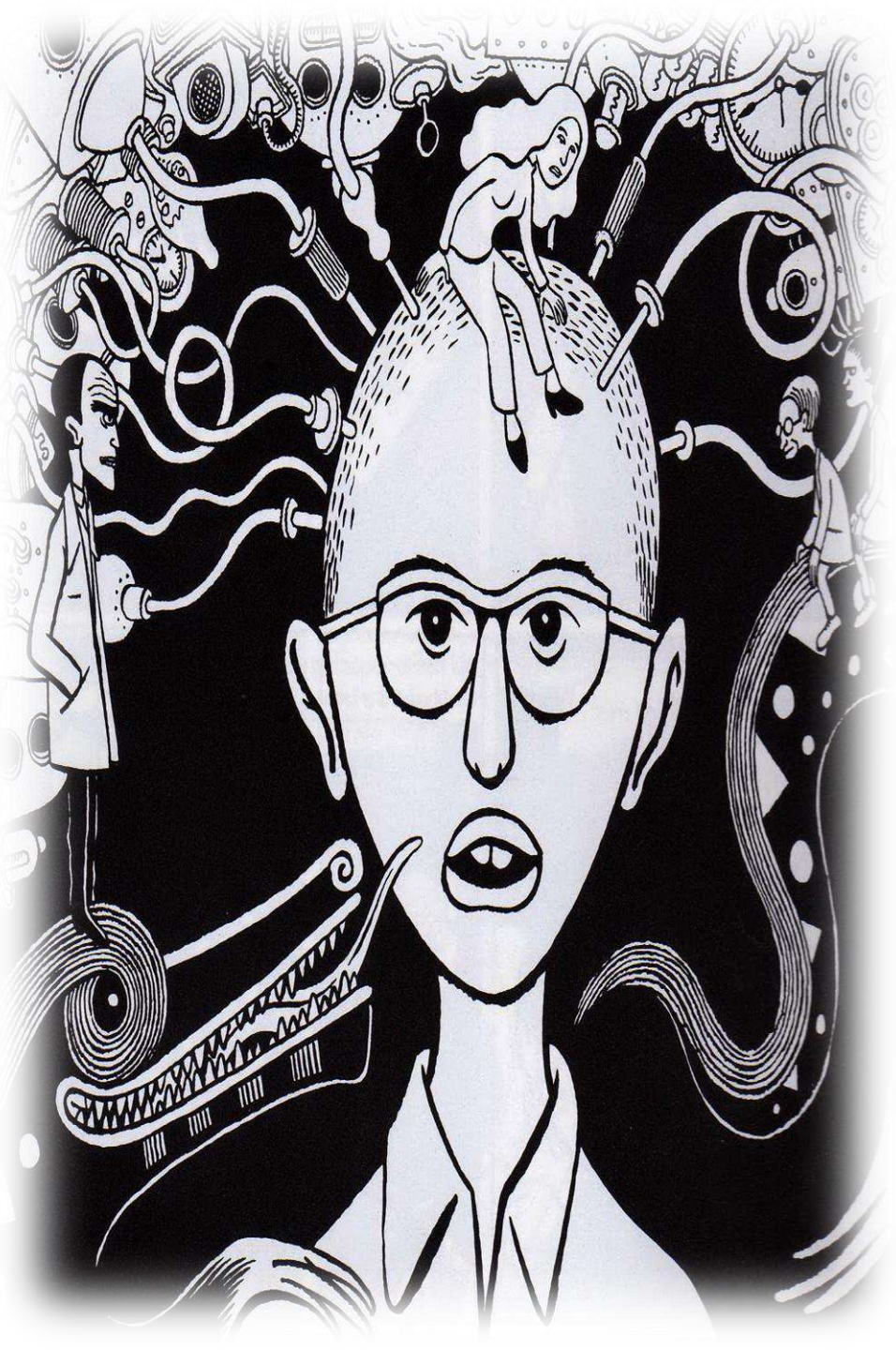
APA, 2013

Disturbance in consciousness

- Reduced clarity of awareness of the environment with reduced ability to focus, sustain or shift attention.

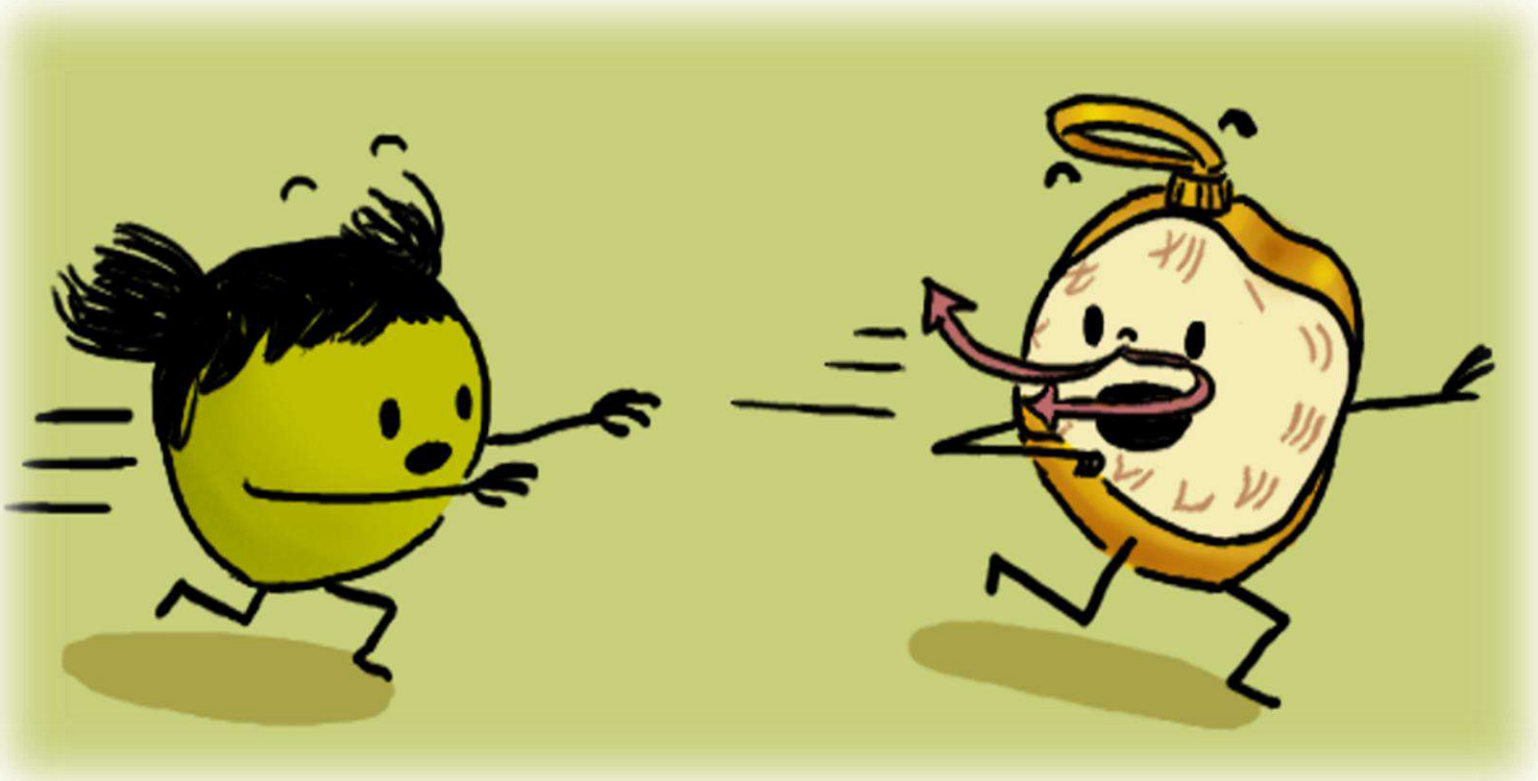
Cognition

- Problem-solving impairment
- Disorientation
- Language disturbance
- Memory deficit
- Perceptual disturbance



fluctuating course

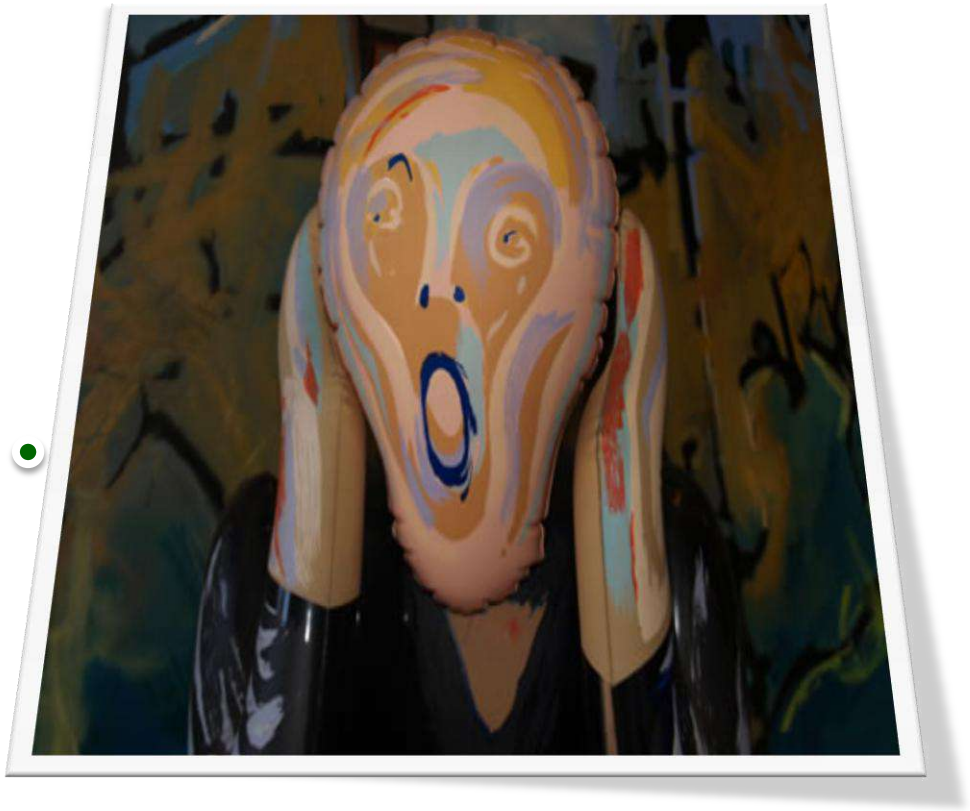
- Onset of hours to days and changes in the sleep/wake cycle



Linkage to a physiologic cause

- ✓ **I** nfection
- ✓ **I** nflammation
- ✓ **N** eoplasia
- ✓ **C** [illegible]
- ✓ **H** ypoxia
- ✓ **D** eficiency eg. Thiamine
- ✓ **E** ndocrine
- ✓ **A** cute vascular
- ✓ **T** oxins and drugs
- ✓ **H** eavy metals

They often may be reversible



Delirium: Causes

1. Illness itself (serious infection or neoplasm)
2. By products of the illness (metabolic or endocrine dysfunction)
3. Side-effects of the treatment (sedative drugs or drug withdrawal)

Delirium: Risk factors

Predisposing risk factors

- ✓ Young age
- ✓ Preexisting cognitive impairment
- ✓ Severity of illness
- ✓ Depression
- ✓ Vision or hearing impairment
- ✓ Functional impairment

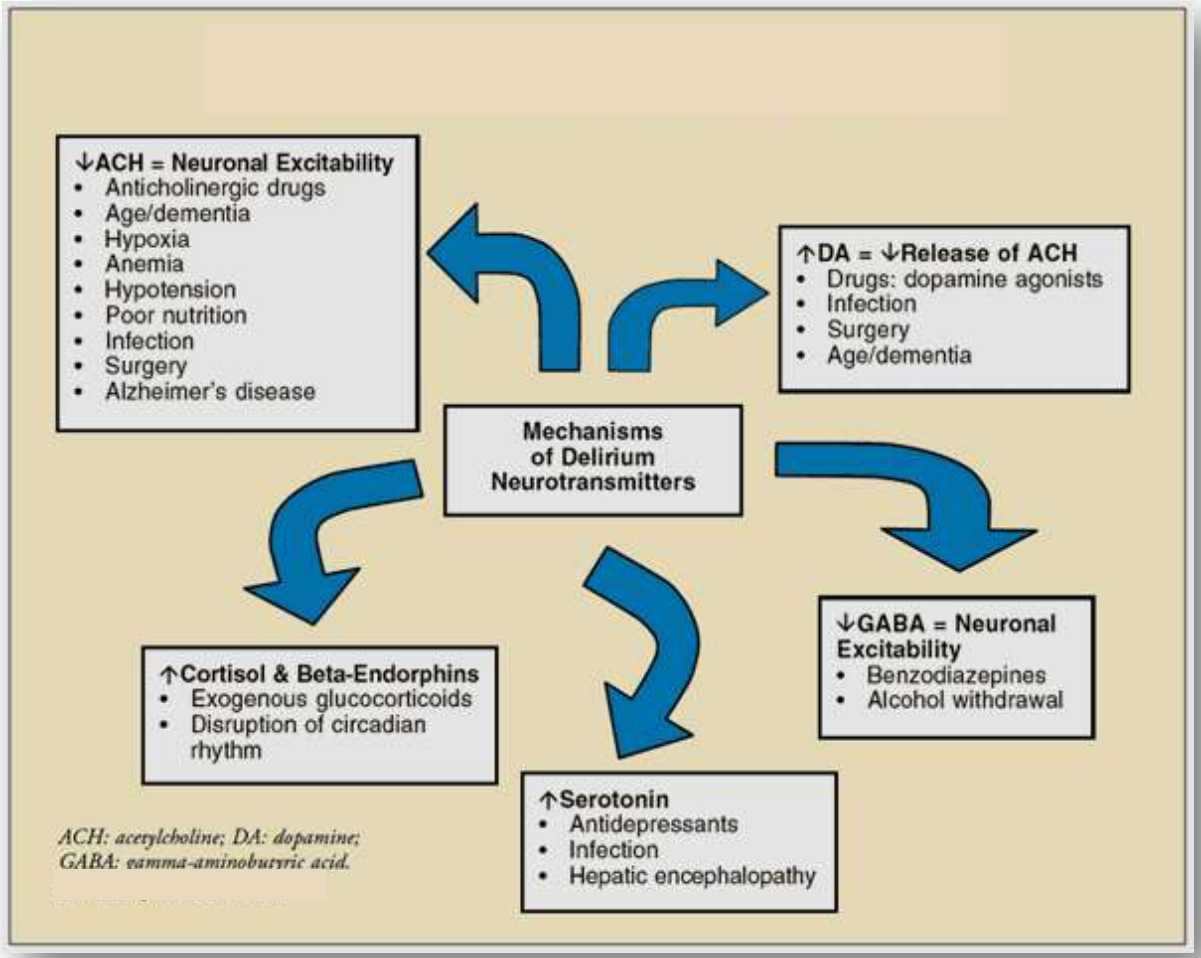
Precipitating risk factors

- ✓ Medication errors
- ✓ Immobilization
- ✓ Dehydration
- ✓ Malnutrition
- ✓ Iatrogenic events
- ✓ Infections
- ✓ Metabolic abnormalities
- ✓ Alcohol or drug withdrawal
- ✓ Psychosocial factors
- ✓ Bladder catheters
- ✓ Physical restraints
- ✓ Sleep deprivation
- ✓ Fecal impaction
- ✓ Urinary retention

Delirium: Pathophysiology

- Delirium has been considered as a nonspecific and stereotyped response of the brain to different aggressions
- It is mediated by a **deficit of acetylcholine** or a **predominance of dopamine**
- In general, neuroimaging studies reveal disruptions in higher cortical functioning in multiple disparate areas of the brain, including the **prefrontal cortex, subcortical structures**, thalamus, basal ganglia, lingual gyri and temporoparietal cortex
- Evidence also points to the role of cytokines such as **interleukins 1 and 2 and TNF-alpha and interferon** in contributing to delirium
- Finally, **chronic hypercortisolism**, as induced by chronic stress secondary to illness or trauma, may also contribute to delirium initiation

Delirium: Pathophysiology



Subtypes of Pediatric Delirium

- **Brain organ dysfunction can manifest as a continuum of psychomotor behaviors that are categorized as hyperactive or hypoactive**

Schieveld J et al.
Intensive Care Med 2007

Diagnosis

- **The ability to mobilize, focus, and sustain attention can be easily appreciated in infants by noting how they engage, make eye contact and remain interested.**

Delirium

- ✓ ***It is more difficult to make the diagnosis in the very young because of the need for experience in the evaluation of behavior and cognition in infants and toddlers (Turkel et al. 2012).***
- ✓ ***Children with delirium may appear to have a more acute onset and more severe symptoms than adults (Leentjens et al. 2010)***


Look See Observe...

Delirium: Screening

- An ideal screen would be simple, quick applicable to children of all ages and cognitive levels and administered by non-psychiatrists…

Assessment scales for delirium: A review

Sandeep Grover, Natasha Kate

World J Psychiatr 2012 August 22; 2(4): 58-70

Table 1 Scales for assessment of delirium in clinical and research setting

Instruments for assessment of arousability of the patient	RASS[9]
Instruments for screening for premorbid cognitive disturbances	IQCODE[10,11]
Screening instruments	NEECHAM Confusion Scale[12]
	Nursing Delirium Screening Scale[13]
	Delirium Observation Screening Scale/Delirium Observation Scale[14,15]
	Intensive care delirium screening checklist[16]
	Pediatric Anesthesia Emergence Delirium scale[17]
	Global Attentiveness Rating[18]
Diagnostic instruments	Delirium Symptom Interview[19]
	Saskatoon Delirium Checklist[20]
	Delirium Rating Scale-revised version[21]
	Memorial Delirium Assessment Scale[22]
	Confusion Assessment Method[23]
	CAM-ICU[24,25]
	Paediatrics CAM-ICU[26]
	Clinical Assessment of Confusion - A and B[27,28]
Instruments for Assessment of severity of delirium	Delirium Rating Scale[29]
	Delirium Rating Scale-Revised-98[21]
	Confusion Assessment Method[23]
	Confusion Assessment Method for Intensive Care Unit assessment tool[24,25]
	Delirium-O-Meter[30]
	Delirium Index[31]
	Memorial Delirium Assessment Scale[22]
	Confusional State Evaluation Scale[32]
	Delirium Assessment Scale[33]
	Delirium Severity Scale[34]
Instruments for assessment of cognitive symptoms only	Mini Mental Status Examination[35]
	Cognitive Test for Delirium[36,37]
	Clock Drawing test[38]
	Digit Span Test[39,40]
	Vigilance "A" Test[41]
	Mental state Questionnaire[41,42]
	Short Portable Mental Status Questionnaire[43]
Motor symptoms	Delirium Motor Checklist, Delirium Motor Symptom Scale[44,45]
	Richmond Agitation and Sedation Scale[9]
	Motoric items of Delirium Rating Scale, Delirium Rating Scale-Revised-98, Memorial Delirium Assessment Scale[21,22,29]
Etiology, risk factors	Delirium Etiology Checklist[46]
Paediatric delirium	Pediatric Anesthesia Emergence Delirium scale[17]
Distress with delirium experience	Delirium Experience Questionnaire[47]

Delirium

- Delirium Rating Scale (DRS)
- Pediatric Confusion Assessment Method for the ICU (pCAM)
- Pediatric Anesthesia Emergence Delirium scale (PAED)
- Cornell Assessment of Pediatric Delirium (CAP-D)

Intensive Care Med (2012) 38:1025–1031
DOI 10.1007/s00134-012-2518-z

PEDIATRIC ORIGINAL

Gabrielle Silver
Chani Traube
Julia Kearney
Daniel Kelly
Margaret J. Yoon
Wendy Nash Moyal
Maalobeeka Gangopadhyay
Huibo Shao
Mary Jo Ward

Detecting pediatric delirium: development of a rapid observational assessment tool

Table 1 Cornell Assessment of Pediatric Delirium (CAP-D)

RASS score _____ (if −4 or −5 do not proceed)						
	Not at all 4	Just a little 3	Quite a bit 2	Very much 1	Extremely 0	Score
1. Does the child make eye contact with the caregiver?[a]						
2. Are the child's actions purposeful?[a]						
3. Is the child aware of his/her surroundings?[a]						
	Not at all 0	Just a little 1	Quite a bit 2	Very much 3	Extremely 4	
4. Is the child restless?[a]						
5. Is the child inconsolable?[a]						
6. Is the child underactive: very little movement and interaction?[b]						
7. Are the child's responses sparse and/or delayed?[b]						
Total (≥10 delirium present)[c]						

RASS Richmond Agitation-Sedation Scale

[a] Elements of the original PAED [29], modified from statement to question form

[b] Questions added to improve detection of hypoactive and mixed delirium

[c] The original PAED was scored: 0–6, no delirium and no further evaluation needed; 7–9, subsyndromal delirium and reevaluate soon; ≥10, delirium present

Developmentally appropriate and language-appropriate bedside

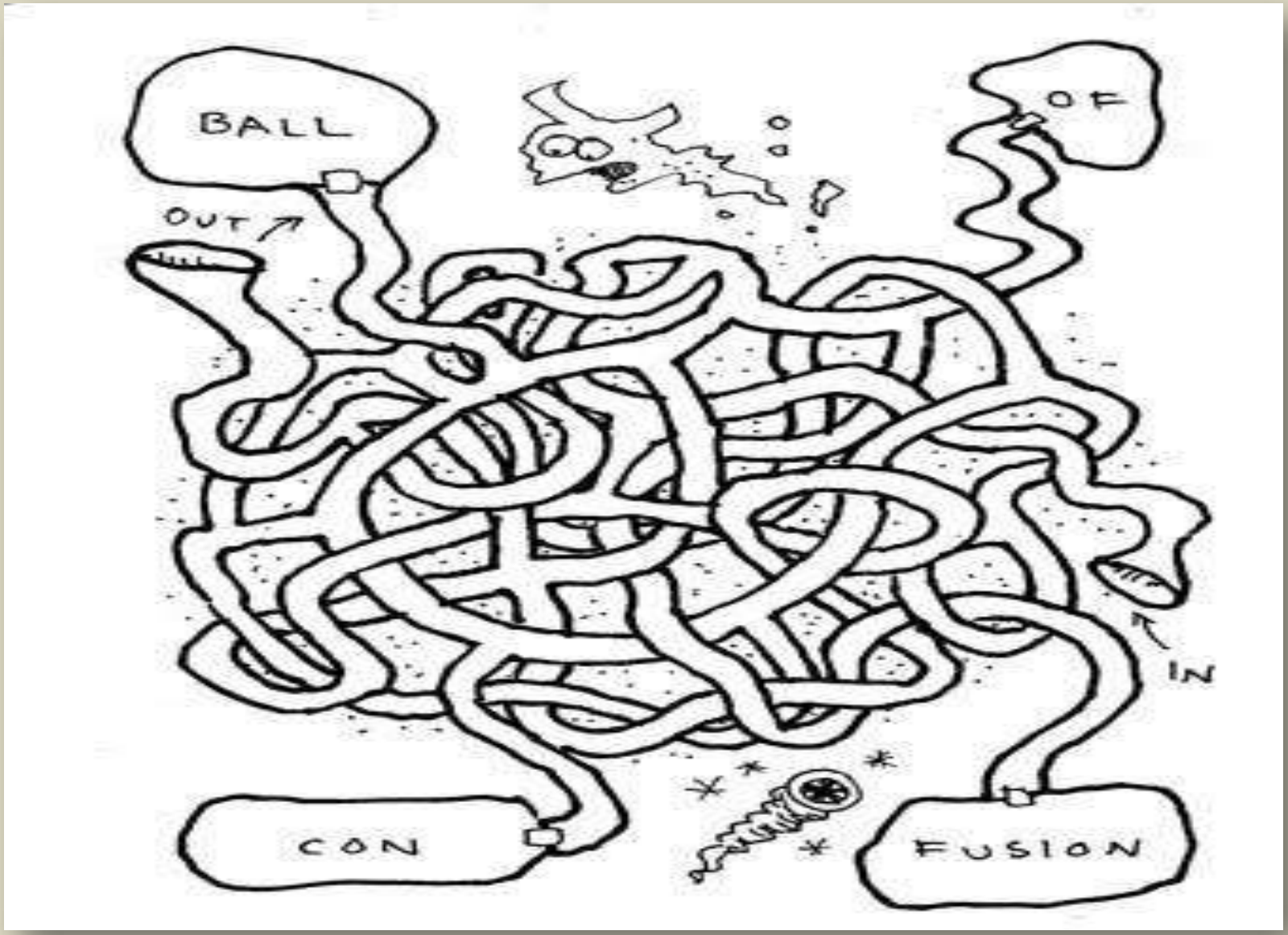


TABLE 1. Selected Cornell Assessment of Pediatric Delirium Developmental Anchor Points and Diagnostic and Statistical Manual IV Delirium Domain Correlates

Cornell Assessment of Pediatric Delirium Item	Diagnostic and Statistical Manual Delirium Domains	Selected Normal Developmental Anchor Points[a]	
		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

[a]Anchor points were developed for newborn and 4 wk, 6 wk, 8 wk, 28 wk, 1 yr, and 2 yr olds.

Delirium: Treatment

- The cardinal component of delirium treatment is first to detect and address its *underlying cause*
- Treatment of PD consists of two components: *psychosocial* (restoring orientation and comfort) and *pharmacological* (antipsychotic) management
- Management practices are based on expert opinion, case series and extrapolation from literature regarding delirium in adults

Non pharmacological management

- Parent/ caregiver presence
- Limit visitors
- Appropriate level of stimulation
- Orienting materials
- Frequent reorientation
- Lighting schedule
- Warm comfortable blanket

Pediatric delirium in the pediatric intensive care unit: a systematic review and an update on key issues and research questions

C. CRETEN [1], S. VAN DER ZWAAN [1*], R. J. BLANKESPOOR [1*], P. L. J. M. LEROY [2], J. N. M. SCHIEVELD [1]

- **Another issue regarding treatment is the importance to recognize the difference and overlap between withdrawal and PD**
- **According to DSM-IV-TR this difference could be just quantitative*. longer, more severe, and more serious* symptoms than might be expected are indicative of PD and not any more of withdrawal**
- **On the other hand nobody knows up until now where the cut-off point is to differentiate exactly between delirium and withdrawal symptoms**

Minerva Anestesiol, 2011

Case Reports

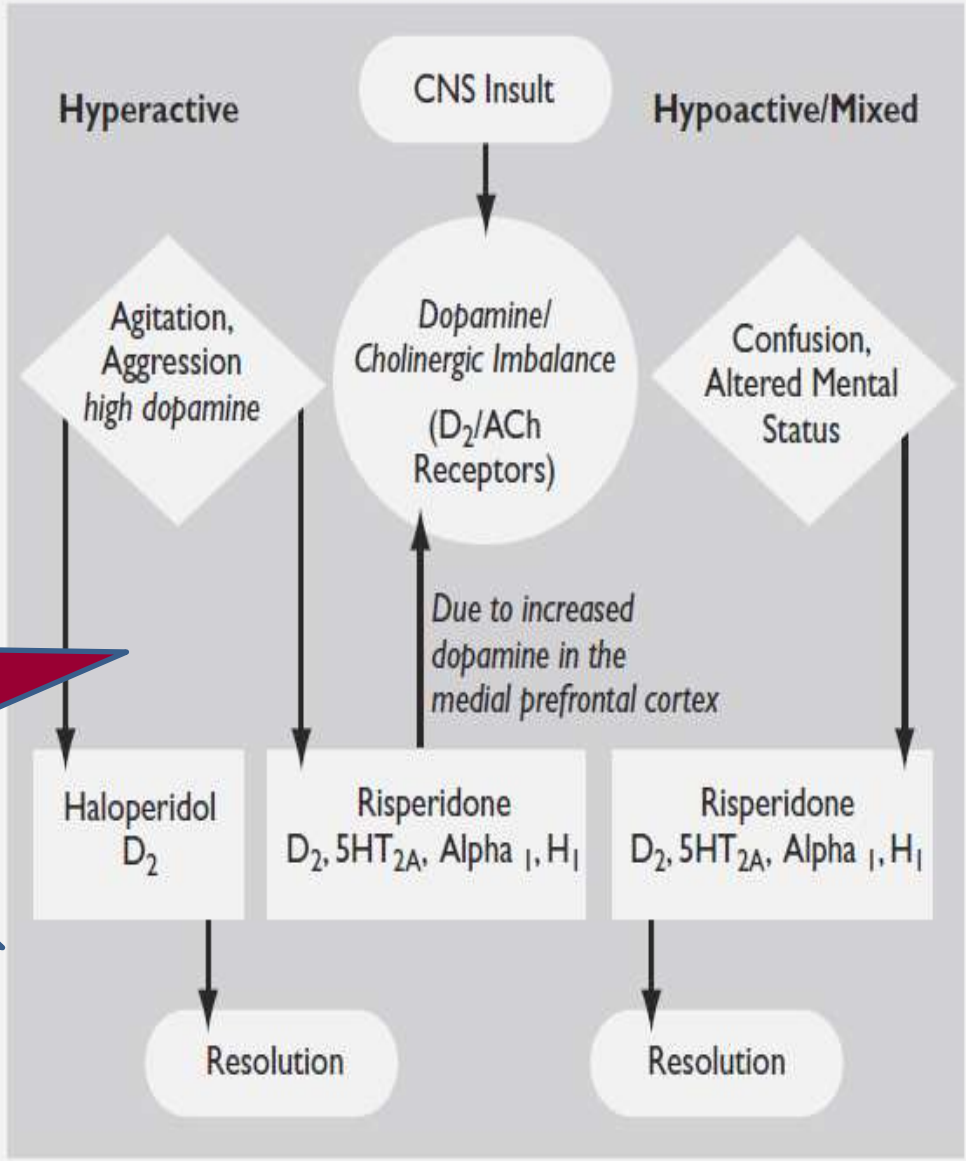
Subtypes of Pediatric Delirium: A Treatment Algorithm

Niranjan S. Karnik, M.D., Ph.D., Shashank V. Joshi, M.D.
Caroline Paterno, B.A., Richard Shaw, M.B., B.S.

Delirium in adult populations of hospitalized patients has been well characterized into hyperactive, hypoactive, and mixed subtypes. The degree to which these subtypes apply to pediatric populations has yet to be fully demonstrated. In this case report, the authors present two cases of delirium that serve as examples of the hyperactive and hypoactive/mixed types and then discuss treatment. They find marked differences in the response of different delirium subtypes to haloperidol and risperidone and theorize as to the neurochemical pathways by which these pharmacological agents might work. This framework provides an algorithm for the treatment of pediatric delirium.
(Psychosomatics 2007; 48:253–257)

It is believed that risperidone has wider receptor effects than haloperidol which relatively narrowly targets the D2 receptor

FIGURE 1. Model for Use in the Treatment of Delirium in Children



Psychopharmacologic Management of Depression, Anxiety, Delirium, and Insomnia in Children. A Palliative Care Perspective

Kimberly Bower et al. Presented at: American Academy of Hospice and Palliative Medicine Annual Assembly; 2011; Vancouver, BC.

Drug	Proposed MOA	Dosing guidelines	Routes of administration	Absorption, metabolism, excretion	Pearls
Haloperidol	Dopamine receptor (D_2) antagonist	Ages 6 - 13 y: 0.05 - 0.5 mg/kg/d in 2 or 3 divided doses Ages 13 - 18 y: 0.5 - 2 mg 2 or 3 times daily Maximum: 100 mg/d Equivalent dosing PO/SC/IM/IV	PO, SC, IV, IM	C_{max}: 2 - 6 h; $T_{\frac{1}{2}}$: 21 h; liver metabolism; renal excretion	Avoid in congenital QT_c prolongation; case reports of use in children as young as 28 mo; increased sedation
Chlorpromazine	5-HT_2 serotonin and D_2 receptor antagonist H1 antagonism significant	Ages 6 - 13 y: 0.55 mg/kg every 4 - 6 h; maximum: 100 - 200 mg/d Ages 13 - 18 y: 25 mg, titrate to 25 - 50 mg/d to effect; maximum: 1000 mg/d up to 2000 mg/d for brief time Equivalent dosing PO/SC/IM/IV	PO, SC, IM, PR	C_{max}: 1 h; $T_{\frac{1}{2}}$: 24 h; liver metabolism; renal excretion	Avoid in congenital QT_c prolongation; increased sedation
Risperidone	5-HT_2 serotonin and D_2 receptor antagonist	Ages 6 - 13 y: 0.01 - 0.06 mg/kg/d; maximum: 2 mg/d Ages 13 - 18 y: 0.5 - 1 mg/d; titrate to 4 - 6 mg/d to effect; maximum: 16 mg/d	PO	Risperidone: C_{max}: 1 - 2 h; $T_{\frac{1}{2}}$: 3 h 9-OH risperidone: C_{max}: 1 - 2 h; $T_{\frac{1}{2}}$: 24 h Liver metabolism and dosing changes; renal dosing changes[a]	Increased sedation; less EPS
Olanzapine	5-HT_2 serotonin and dopaminergic D_2 receptor antagonist; H1 antagonism significant	Ages 13 - 18 y: 2.5 mg/d; titrate to 5 - 10 mg/d in 2 divided doses; maximum: 20 mg/d	PO, SC, IM	C_{max}: PO, 6 h; SC, 30 min; $T_{\frac{1}{2}}$: 30 h; liver metabolism; renal excretion	Increased sedation
Quetiapine	Potent serotonin 5-HT_2 with moderate D_2 receptor antagonism	Ages 10 - 18 y: 25 mg twice daily; titrate to effect; maximum: 600 mg/d (aged > 10 y); 800 mg/d (closely monitored adolescents)	PO	C_{max}: 1.5 h; $T_{\frac{1}{2}}$: 6 h; liver metabolism; renal excretion	Increased sedation; less EPS; suicidal ideation in children and adolescents

Palliative Medicine 2004; **18:** 184–194

Delirium in advanced cancer patients

Carlos Centeno Centro Regional de Cuidados Paliativos y Tratamiento del Dolor, Hospital Los Montalvos, Salamanca, **Álvaro Sanz** Servicio de Oncología, Hospital Clínico Universitario, Valladolid and **Eduardo Bruera** Department of Palliative and Rehabilitation Medicine, The University of Texas, MD Anderson Cancer Center, Houston, TX

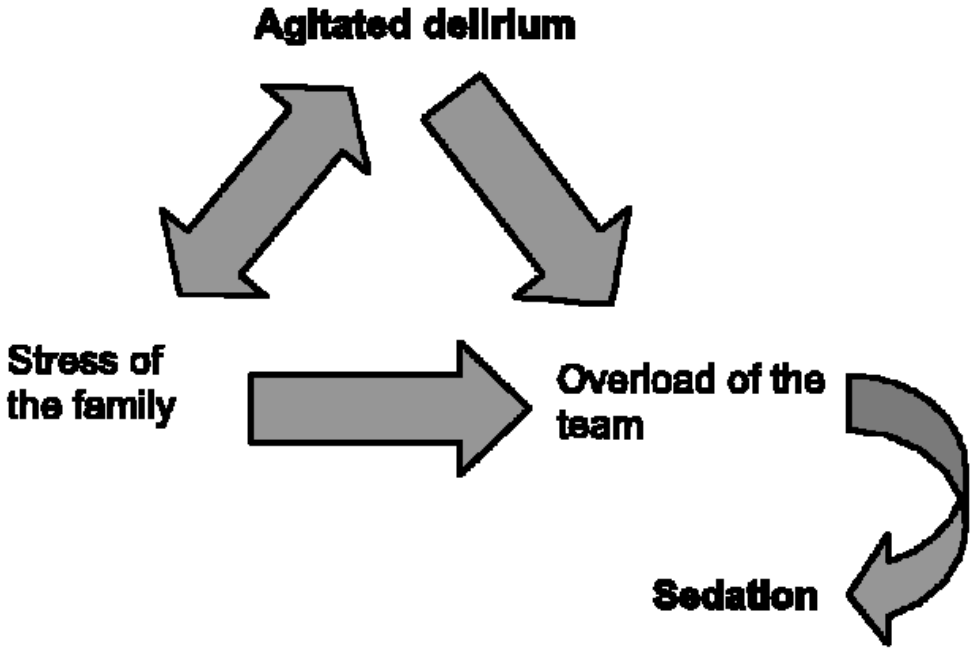
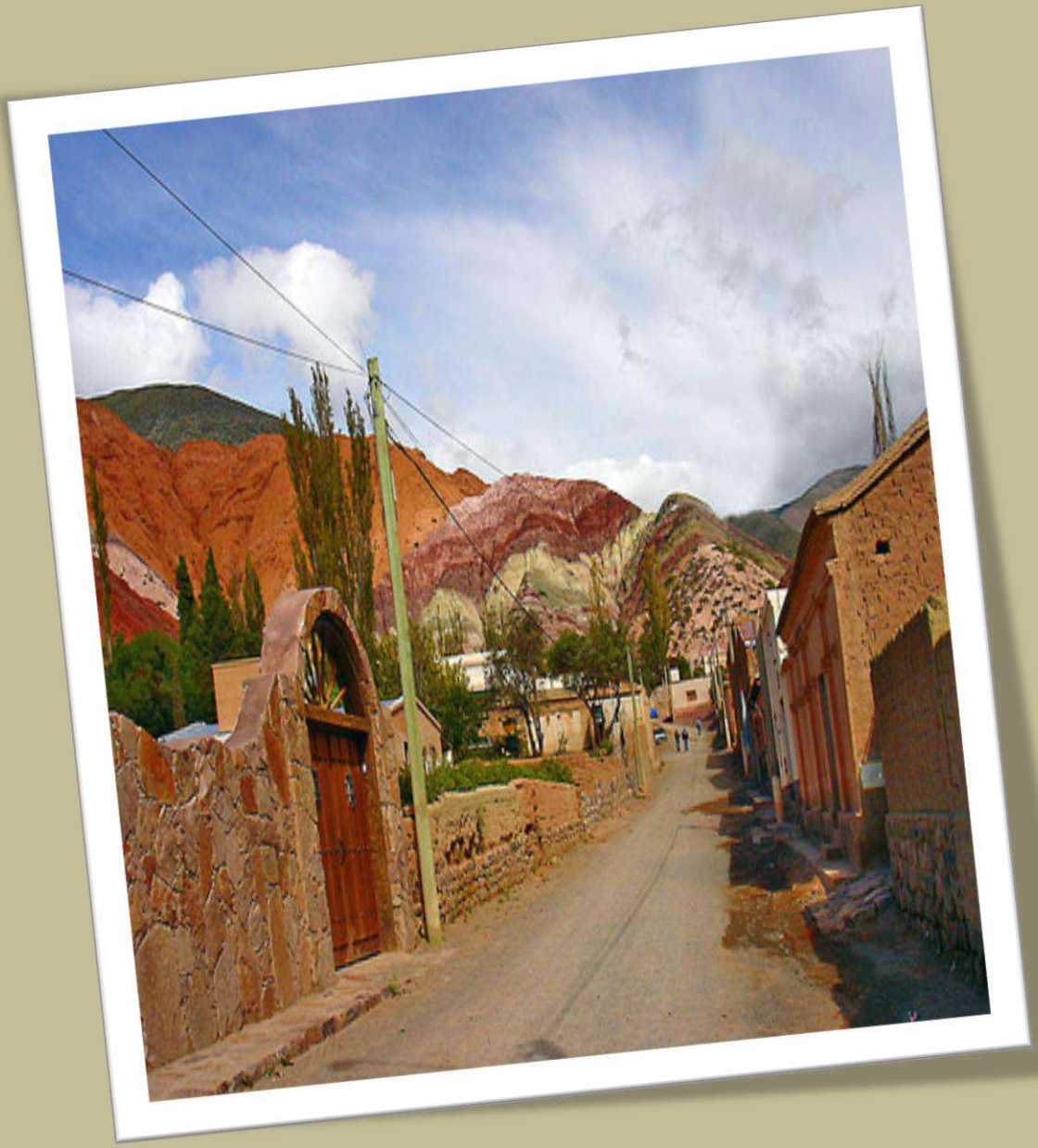


Figure 1 Sedation as a consequence of a noncontrolled agitated delirium, influenced by delirium-induced stress of proxies and overload in therapeutic team ('destructive triangle').

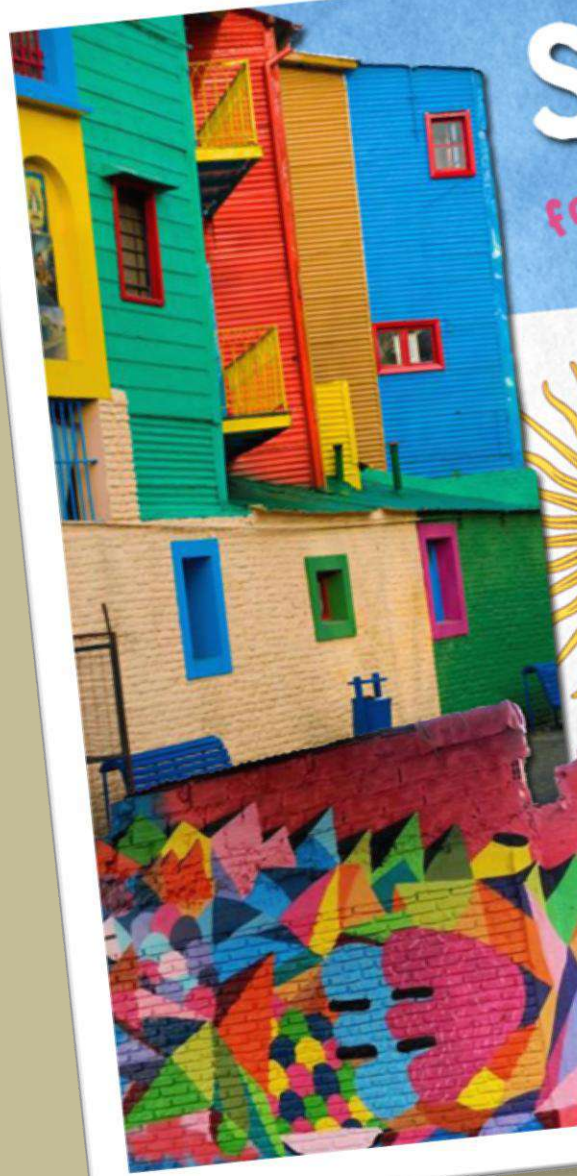
Conclusions

- ✓ PD is an important but neglected disorder
- ✓ Delirium is defined as a transient, usually reversible, cause of cerebral dysfunction and manifests clinically with a wide range of neuropsychiatric abnormalities
- ✓ The diagnosis of delirium is clinical. No laboratory test can diagnose delirium
- ✓ Of the 3 subtypes of delirium (hypoactive, hyperactive, and mixed), hypoactive is frequently mistaken for depression
- ✓ It is associated with significant morbidity and high mortality
- ✓ Clinical practice for management is based on limited empirical evidence
- ✓ These conditions cause significant distress for not only the patient, but also the family and care team



Thanks you for your attention!!!

rkiman@gmail.com



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