Pediatric Delirium
Monitoring and Management in the Pediatric Intensive Care Unit

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KEYWORDS
- Delirium • Brain dysfunction • Encephalopathy • Sedation • Agitation • Pain • Critical care • Pediatric

KEY POINTS
- Pediatric delirium (acute brain dysfunction) can be a complication of critical illness.
- Brain organ dysfunction can manifest as a continuum of psychomotor behaviors that are categorized as hyperactive or hypoactive.
- Delirium can be diagnosed using validated and reliable bedside tools.
- Implementation of delirium monitoring can be enhanced by scheduled in-depth discussions about brain organ dysfunction via multidisciplinary rounds with the medical team.
- Pediatric delirium may be managed with use of nonpharmacologic and, if necessary, pharmacologic interventions thereafter.
INTRODUCTION: PEDIATRIC DELIRIUM

Children suffer from delirium during critical illness in a similar manner to adults. The efficient diagnosis of pediatric delirium has recently evolved with the availability of valid and reliable bedside tools, although research in this field remains in its infancy. The use of valid delirium-monitoring tools and large-scale delirium-monitoring implementation projects have established the prevalence of delirium in critically ill adults to be between 40% and 80%, with a significant association with increase in length of ventilation, length and costs of hospitalization, and greater mortality, after adjusting for severity of illness. Furthermore, survivors of critical illness who have suffered from delirium have been predisposed to long-term cognitive impairment (LTCI) and posttraumatic stress disorder (PTSD). By contrast, pediatric delirium occurs in at least 30% of critically ill children, with worse clinical outcomes as described in limited retrospective reports. The long-term complications of critical illness and delirium in children remains uncertain, although preliminary studies comparing hospitalized children with those admitted to the pediatric intensive care unit (PICU) demonstrate critical illness to be associated with decreases in spatial and verbal memory and sustained attention. Critically ill children are also more likely to have significantly longer school absences following discharge to home. LTCI following critical illness may impair executive function, an aspect of brain function that is required for purposeful, goal-directed, and problem-solving behavior, such as that required for higher learning. It remains unclear whether the severity of illness associated with critical illness, components of critical illness (eg, diagnosis such as sepsis and cardiac surgery), or its management (eg, delirium, medications administered, metabolic disturbances, hypoxemia) predispose patients to these long-term complications.

Despite the recognition of high prevalence rates of delirium in adults and children, and the associations of adverse outcomes with delirium in adults (some reported cases in children too), there remains a hesitation within the pediatric critical care community to embrace delirium monitoring and therapy, because of ongoing reservations regarding the clinical diagnosis, symptomatology, and pathophysiology. This uncertainty is complicated by a lack of clear treatment options within the pediatric medical literature. For many clinicians, delirium remains an expected and trivial component of illness. This article presents a brief overview of pediatric delirium and proposes a model for implementation of delirium monitoring, along with an initial approach to management.

DEFINITION

Delirium (conceptualized as acute brain dysfunction) is defined in the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders fourth edition, text revision (DSM-IV-TR) as a disturbance of consciousness and cognition that develops acutely with a fluctuating course of mental status, inattention, and an impaired ability to receive, process, store, or recall information, directly triggered by a general medical condition. Delirium has been described using many terms such as intensive care unit (ICU) psychosis, ICU syndrome, acute confusional state, encephalopathy, and acute brain failure. A great emphasis therefore needs to be placed on the accurate diagnosis of pediatric delirium within the medical literature and in clinical practice.

DIAGNOSIS OF DELIRIUM

Historically, diagnosis of delirium has relied on formal evaluation by an expert in psychiatry or neurology using DSM-IV-TR criteria. Unlike other types of organ dysfunction

1. INTRODUCTION: PEDIATRIC DELIRIUM
2. DEFINITION
3. DIAGNOSIS OF DELIRIUM
that can be diagnosed by a blood test or monitoring system, diagnosis of delirium currently requires a complete medical examination of the patient, including both careful neurologic evaluation and assessment of mental status. A formal expert consultation is extensive, requiring significant time available to the consultant for a complete physical examination and evaluation of the patient’s history and clinical course. Relying on expert consultation alone for delirium monitoring would be impractical for the PICU setting. Pediatric delirium can present with neuropsychiatric symptoms similar to those observed in adults, such as sleep-wake disturbances, disorientation, and inattention. Unique features including purposeless actions, labile affect, inconsolability, and signs of autonomic dysregulation may occur more frequently with pediatric delirium, specifically related to the developmental stage of the child. 15,29 The variation in clinical presentation and cognitive development between children and adults highlights the benefit of pediatric focused diagnostic approaches to delirium. 1,16,30,31

The Pediatric Confusion Assessment Method for the ICU (pCAM-ICU) was created and successfully validated (specificity 99%, sensitivity 83%) for the diagnosis of delirium against formal neuropsychiatric reference raters in critically ill children older than 5 years, both on and off mechanical ventilation (Fig. 1). 1 In the adult population, several screening tools have become standards for delirium monitoring in the hospital and ICU settings, including the Delirium Rating Scale (DRS), 32 Confusion Assessment Method for the ICU (CAM-ICU), 4,33 and the Intensive Care Delirium Screening Checklist (ICDSC). 5 The pCAM-ICU was adapted from the CAM-ICU because of the need for objective and interactive patient assessments focusing on the cardinal features of delirium, including altered or fluctuating mental status and inattention. 1,4,21,33 The hierarchical construction of the pCAM-ICU allows for the evaluation of the most fundamental features of delirium first. If either fluctuation or acute change in mental status (feature 1) or inattention (feature 2) are not present, delirium is absent. Delirium is present when patients demonstrate having both features 1 and 2, followed by either feature 3 or feature 4. 1,4,33 The pCAM-ICU allows for a rapid assessment of delirium, taking less than 2 minutes to complete. The structure of pCAM-ICU algorithm is efficient and is focused on those symptoms most consistent with delirium.

The Corneal Assessment of Pediatric Delirium (CAP-D), 2 a delirium-monitoring tool that has been shown to be valid and reliable for the evaluation of delirium in infants and children, is a modification of the Pediatric Anesthesia Emergence Delirium (PAED) scale. 34 The CAP-D added components to the basic structure of the PAED to increase the likelihood of detecting hypoactive delirium, as the PAED was originally created to recognize emergence delirium, a severe form of hyperactive delirium in the postanesthesia setting. The PAED and CAP-D rely heavily on observation versus patient-caregiver interaction. The developmental and cognitive changes that occur between infancy and childhood are not specifically taken into consideration with either tool. The cardinal features of delirium, such as inattention, are not awarded more weight toward the final score for the diagnosis of delirium in the CAP-D. Rather, all 7 components of the scale have to be completed and have equal value for the determination of delirium.

A limitation for delirium monitoring in pediatric patients is the presence of progressive changes in development and cognition that occurs from infancy to young childhood, and ultimately through adolescence. Tool development must factor in the variable capacity for communication of attention and thought content based on age and stage of development, resulting in the need for more than 1 simple tool for use on all pediatric patients. The pCAM-ICU has been adapted to the PreSchool Confusion Assessment Method for the ICU (psCAM-ICU), which accounts for these unique differences in pediatric patients and is presently being validated at Vanderbilt for use in infants as young as 6 months and children up to 5 years of age. This tool was created
Pediatric Confusion Assessment Method for the ICU (pCAM-ICU)

1. **Acute Change or Fluctuating Course of Mental Status**
   - Is there an acute change from mental status baseline? **OR**
   - Has the patient’s mental status fluctuated during the past 24 hours?
   
   May use GCS, sedation scale, exam, or history to answer either question.

2. **Inattention → Attention Screening Examination (ASE) with Letters or Memory Pictures**
   - Say: “Squeeze my hand when I say ‘A’. Let’s practice: A, B. Squeeze only on A.”
   
   Read this letter sequence: A B A D B A D A Y
   
   **Letter Errors**: No squeeze with ‘A’ or squeeze with letter other than ‘A’.
   
   **Picture Errors**: “No” with memory picture or “Yes” with other picture

3. **Altered Level of Consciousness**
   - Is the patient currently ALERT and CALM? (RASS, MMAAS, SBS → Score 0)
   
4. **Disorganized Thinking → 5 tasks to include 4 questions and 1 command.**
   - Say: “I am going to ask you some questions. Say or nod ‘yes or no’ to answer each question.”
   
   1) Is sugar sweet?  
   2) Is ice cream hot?  
   3) Do birds fly?  
   4) Is an ant bigger than an elephant?  
   5) **Command**: “Hold up this many fingers” (Demonstrate by holding up 2 fingers)

   “Now do that with the other hand,” **OR** “Add one more finger” (No demonstration)

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Fig. 1. Pediatric delirium assessment tool: Pediatric Confusion Assessment Method for the ICU (pCAM-ICU). The pCAM-ICU is a valid and reliable tool for diagnosing delirium in critically ill children at least 5 years old. Patients with an acute change or fluctuation from baseline mental status (feature 1) AND inattention (feature 2) with either an acute alteration in level of consciousness (feature 3) OR disorganized thinking (feature 4) have delirium. (Courtesy of Heidi A.B. Smith, MD, MSCI, Nashville, TN; and From Smith HA, Boyd J, Fuchs DC, et al. Diagnosing delirium in critically ill children: validity and reliability of the Pediatric Confusion Assessment Method for the Intensive Care Unit. Crit Care Med 2011;39:152, with permission.)
with an expert panel of board-certified pediatric psychologists, neurologists, developmental pediatricians, anesthesiologists, intensivists, and child and adolescent psychiatrists. Furthermore, valid tools to assess pediatric neurocognition, pain and behavior, and developmental milestones were used as a guide to ensure that the cognitive and consciousness assessments within the psCAM-ICU were appropriate for infants and young children. As with the CAM-ICU and pCAM-ICU, the psCAM-ICU places emphasis on the most fundamental features of delirium: acute changes or fluctuations from baseline mental status and inattention.

ETIOLOGY AND PRESENTATION OF DELIRIUM

Delirium can have a variety of presentations, ranging from an inappropriately sedate, to calm, or agitated patient who does not rest, may resist care, and becomes withdrawn from family or familiar items. Delirium is categorized into subtypes based on these presenting psychomotor behaviors as hypoactive, hyperactive, or a mixed type. Normal brain activity depends on a fragile balance of stimulatory and inhibitory neurotransmission that becomes disrupted because of a variety of central nervous system insults occurring during critical illness. Aberrant neurotransmission (delirium) in key areas of the brain is demonstrated as an acute change in mental status, inattention, and altered level of consciousness or cognition, which all forms of delirium (hypoactive, hyperactive, mixed) have in common.

The psychomotor responses of patients with delirium are due to an alteration of activity at specific brain receptors within the dopaminergic, cholinergic, and glutamatergic systems. Dopamine is a major stimulatory neurotransmitter, whereas acetylcholine and \( \gamma \)-aminobutyric acid (GABA) have inhibitory effects. The balance of both neurotransmitter and receptor action modulate behavior and contribute to the fluctuation of mood, with additional effects on cognitive function.

Hypoactive delirium may be clinically apparent when patients suffer from a significant deficiency of dopamine or an excess of acetylcholine or GABA\( _A \) receptor stimulation. Hypoactive delirium is demonstrated in a patient through apathy, a depressed level of consciousness, and withdrawal from their environment. Unfortunately, these patients rarely arouse concern by the medical team, as they are easily paired and depicted as “good patients,” and this mistaken sense of well-being results in a greater likelihood of poorer outcomes. Patients fluctuating between hypoactive and hyperactive delirium (mixed type) and hypoactive delirium alone are the most commonly observed during critical illness.

Hyperactive delirium may be present when there is an excess of dopaminergic activity and acetylcholine antagonism. The dysfunctional state of hyperactive delirium has been well described in the literature using examples of the anticholinergic toxidrome or dopamine excess, which trigger agitation, restlessness, emotional instability and, ultimately, psychosis. Other presentations of delirium have been observed during critical illness, resulting from the scarcity of acetylcholine and commonly used PICU drugs that have anticholinergic properties. It remains vital for clinicians to understand the GABAergic system, as many of the most commonly used sedatives in the PICU setting, such as benzodiazepines and propofol, stimulate GABA\( _A \) receptors causing sedation, anxiolysis, and even drug-induced delirium and coma.

IMPLEMENTATION OF DELIRIUM MONITORING

There are many obstacles to the institution of a new philosophy, protocol, or monitoring system within the PICU. The bedside nurse is inundated with numerous tasks related to both patient care and hospital protocols/policies. The success of
implementing delirium monitoring in the PICU depends on the medical team’s understanding of the importance, presentation, etiology, and treatment options for delirium, the appreciation of the role of psychiatric or neurology consultation, and the development of confidence that diagnosis of delirium will lead to a change in patient care by the physician. In the early stages of implementation for delirium monitoring at Vanderbilt, in addition to educational in-services and one-on-one training of health care providers, the authors created an opportunity for the education of both physicians and nurses during medical rounds once weekly, with the additional presence of child and adolescent psychiatrist and pediatric anesthesiologists, as well as intensivists with expertise on delirium. The goals for “Brain Rounds” focused on how to redefine the approach to patients within the PICU, recognizing that the overall practice may be deficient in how one diagnoses and manages neurologic, psychiatric, and psychological disease. As an intensivist, the focus of critical care management remains on other vital organ systems (heart, lung, kidneys, and so forth) whereby there is a greater comfort level with diagnosis and treatment. The vast amount of data accumulated on delirium in critically ill adults encourages a transition from the status quo toward a culture change in the PICU for the recognition and management of delirium or brain organ dysfunction in children.

The authors developed Brain Rounds as an opportunity to instruct the medical team on the following: (1) how to identify, describe, and monitor for delirium; (2) how to structure a neuropsychiatric assessment and consider premorbid factors; (3) understand the known risks factors and outcomes for delirium; and (4) how to model

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**Fig. 2.** Alteration in neurotransmission leading to psychomotor disturbance in delirium: the psychomotor responses of patients with delirium resulting from aberrant activity at specific brain receptors within the dopaminergic, cholinergic, and glutamatergic systems. Hyperactive delirium may be observed with an excess of dopaminergic activity and acetylcholine antagonism, resulting in agitation, restlessness, emotional instability, and, ultimately, psychosis. Hypoactive delirium may be clinically evident with a significant deficiency of dopamine or an excess of acetylcholine or \( \gamma \)-aminobutyric acid (GABA\(_A\)) receptor activity, demonstrated as patient apathy, depressed level of consciousness, and withdrawal from the environment. RASS, Richmond Agitation-Sedation Scale. (Data from Karnik NS, Joshi SV, Paterno C, et al. Subtypes of Pediatric Delirium: A treatment Algorithm. Psychosomatics 2007;48:255.)
interdisciplinary thought regarding management. A case-based approach was used for delirium education grounded in educational theory. Case-based learning is a technique that guides the learner in practical application of new knowledge. Clinical rounds are designed to provide service to the patients, and teaching to the learners on the medical team. The importance of good clinical management of children with delirium was used in the context of challenging trainees and faculty to expand their knowledge base regarding pediatric delirium. Brain Rounds was successful because content experts with knowledge of the presentation, diagnosis, risks, and management of delirium were available to assure consistency in instruction and provide a role model for integrated patient care.

Brain Rounds provides an opportunity to identify specific aspects of delirium education that require further clarification, which are then used as beneficial learning points for new team members. At Vanderbilt, the authors were fortunate to delineate misperceptions held by the medical team that were preliminary obstacles to delirium monitoring and management.

Myth 1: The need for a delirium tool is not necessary.

Pediatric physicians and nurses take specific care to prevent a child from undergoing further harm in the PICU setting during critical illness. The recent focus on the occurrence of delirium in the authors’ PICU challenges the assumption that we already know patients’ mental status and cognition well. Delirium tools facilitate the neurologic examination to uncover the key features of delirium that would otherwise potentially be missed.

Myth 2: Delirium monitoring will not lead to a change in patient care.

Management of delirium requires reassessment of sedation and analgesia practices in the PICU setting, which can be viewed as destabilizing by team members, making intentional and consistent change difficult. This inconsistency leads to ineffective delirium management, contributing to the belief that monitoring of delirium will not lead to a change in patient care. Culture change promoted by the clinical team through intentional changes in patterns of behavior within the PICU is needed for delirium management to be successful.

Myth 3: Delirium management requires the removal of all sedatives, leading to awake and suffering patients.

Many providers use significant doses of both analgesics and sedatives in critically ill children, hoping to avoid the creation of distressing memories of the PICU experience. The safety of this practice is challenged by literature that identifies not only the development of delirium more often in adults exposed to benzodiazepines during critical illness but also that children who receive excessive sedation are more likely to have distorted memories of their experience that are associated with the development of PTSD following discharge from the hospital. Medical literature on delirium challenges the caregiver to transition from feeling frustrated over new recommendations for titration of certain drugs, to feeling empowered in having the tools necessary to successfully identify patient needs in regard of pain and anxiety, level of sedation, and delirium. The goal of delirium management is achieved when a child is without significant pain, has adequate anxiolysis via both pharmacologic and nonpharmacologic means using targeted therapy, and responds to treatment of both delirium and the disease state. This approach may result in a child who “experiences” critical illness but without the hurt and fear that we all perceive.
Myth 4: A diagnosis of delirium and psychiatry consultation suggest that the medical team considers the patient “crazy,” and management requires “antipsychotics” for an extended period of time.

Delirium differs very little from other types of organ dysfunction in the collaborative approach to monitoring and therapy. As an example, when a child presents with septic shock, the development of acute renal failure is not unexpected. If severe enough, a nephrologist may be consulted to participate in generating strategies for the prevention of worsening kidney function. Aminoglycosides used in the setting of normal renal function requires only monitoring of drug levels; however, with renal insufficiency the kidney is more at risk for further damage, therefore dose or choice of using the drug is reconsidered, often leading to consultation from the specialty service. On discharge from the hospital, renal function usually returns, and ongoing intervention or monitoring by the nephrology service is no longer needed. Similarly, psychiatrists can provide assistance on considering ways to decrease the risk or severity of delirium beyond treatment of the critical disease. This assistance may involve help with the differential diagnosis, identification of risk factors, modifications of ongoing therapy, and in some instances pharmacologic suggestions. In addition, their knowledge regarding the treatment of pain, anxiety, depression, and sleep disturbances can provide an organized and consistent approach to management. The psychiatrist remains a consistent presence for the monitoring of improvement in delirium symptoms and weaning of pharmacotherapy through discharge. The need for the psychiatrist coincides with the acuity and severity of the clinical presentation of delirium.

Brain Rounds offers a tremendous opportunity to discuss real issues and provide key teaching points and procedures to overcome misperceptions that affect the implementation of delirium monitoring in the PICU. A systematic approach to case-based teaching during Brain Rounds including use of consistent information regarding assessment and management, specific patient-based examples, and clinical role modeling has been successful in creating a delirium-monitoring program in the PICU.

TREATMENT

Delirium management requires a global approach to patient care from the environment we create to the cellular disease process we treat. Through the experiences offered from Brain Rounds, the authors developed a systematic approach to delirium monitoring and management that works in their PICU. The concept of the “Pediatric Road Map” was adapted from the adult delirium group at Vanderbilt to promote the monitoring of pain and anxiety, level of consciousness, and delirium in the PICU, with a guide to a disciplined approach for delirium management. The Pediatric Road Map empowers the nursing staff to observe, report, and discuss the patient’s neuropsychological state by creating a “map” using answers to the following questions: (1) Where is my patient now? (2) How did we get here? (3) Where is my patient expected to go? and (4) How do we get them there? To accomplish this, patients are monitored at appropriate intervals for pain using a validated pain scale, for their level of consciousness via the Richmond Agitation-Sedation Scale (RASS) or other validated sedation scales, and for delirium using the pCAM-ICU in children older than 5 years. On clinical rounds with the medical team, the nurse or physician in-training presents the current RASS and pCAM-ICU (brain organ assessment) with pain
assessment (Where is my patient now?), discusses ongoing therapies and medical conditions that might contribute to that assessment (How did we get here?), then outlines the target RASS and clinical goals for the disease state (Where is my patient expected to go?), followed by creation of a clinical plan of how to successfully titrate therapy that is mutually beneficial for both improvement of critical illness and resolution or prevention of delirium, pain, and anxiety (How do we get them there?).

The Pediatric Road Map uses level of consciousness as a marker to determine the approach for delirium prevention and management. The authors use the RASS (Fig. 3) because it provides an objective evaluation of the level of consciousness, separating verbal from physical stimuli via a logical 3-step process: (1) look, (2) talk, and then (3) touch the patient. Furthermore, each RASS score depicts a very distinct level of consciousness that can be easily targeted and attained through titration of medications. A change in RASS score may also alert the medical team to an unexpected change in brain function, whether it is a product of a change in sedative/analgesic administration or attributable to a new medical process such as a metabolic derangement. The targeted level of consciousness for patients is set at zero (alert and calm) unless there are factors that warrant a more “sedate” patient. The greatest need for sedation is when patients are on mechanical ventilation, with severe lung disease, and patient-ventilator synchrony is required. The provider should be challenged to determine the minimal level of sedation required to keep the patient comfortable and to tolerate mechanical ventilation, and to maintain adequate oxygenation; no assumption should be made that deep sedation is “necessary.” It is easy to use sedation as a mechanism of pharmacologic restraint, and the Pediatric Road Map challenges the medical team to consistently reevaluate the need and target of sedation.

The management of delirium in critically ill children can be generally approached by first assigning patients to one of two groups based on their level of consciousness: (1) comatose or severely obtunded without response to voice (RASS/C0 5, /C0 4), or (2) arousable to voice (RASS/C0 3 to /C0 4). These two groups vastly differ in the degree of altered state of arousal, and the inability to assess the content of consciousness (delirium) in patients whose depressed arousal prevents any response to voice.

The care of comatose or severely obtunded patients can be challenging for the medical team. Evaluation for delirium cannot occur in obtunded or comatose patients, as the neurologic responsiveness required for delirium assessment is lost or minimally present; this does not mean that delirium is absent, only that one cannot clinically diagnose its presence using the pCAM-ICU or any other delirium tool while the patient is comatose. When patients demonstrate a severely depressed level of consciousness, great effort should be exercised in considering possible causes, and therapies that may improve the patient’s mental status (Fig. 4). This goal may be achieved through the treatment of possible contributing causes (the acronym BRAIN MAPS; see Fig. 4), the assessment and targeting of a specific level of consciousness to which psychotropic medications are titrated to reach, and the initiation of preventive measures to decrease the likelihood of ongoing delirium when the patient’s sensorium improves. The Pediatric Road Map assists the medical team in consistently reevaluating patients with coma and minimizing risks for the development of delirium while the brain is experiencing an acute state of critical illness.

The care of critically ill patients who are arousable is augmented by the medical team’s ability to monitor for pain, anxiety, and delirium. Delirium assessment can be performed accurately using the pCAM-ICU in intubated or nonintubated children 5 years of age and older who are at least arousable to voice (RASS −3 to +4). When delirium is diagnosed, the subtype (hypoactive, hyperactive, mixed) can be determined by the psychomotor behaviors demonstrated by the patient (apathy and
Fig. 3. Targeting the level of consciousness (LOC) using the Richmond Agitation-Sedation Scale (RASS). The RASS is a valid tool for the objective assessment of the level of consciousness. The clinician first observes whether the patient is alert and calm (RASS 0) or demonstrates mild to severe levels of agitation (RASS +1 to +4). If the patient is not alert and calm nor agitated, then the clinician “talks” to the patient to assess mild to moderate levels of depressed consciousness (RASS –1 to –3). If the patient has no response to voice, then the clinician “-touches” the patient to elicit either some minimal response (RASS –4) or no response because the patient is comatose (RASS –5). *(Data from* Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation–Sedation Scale Validity and Reliability in Adult Intensive Care Unit Patients. *Am J Respir Crit Care Med* 2002;166:1339.)
lethargy, calm, agitation) or the level of consciousness as determined by the RASS, which helps to guide initial management (Fig. 5). The approach to delirium management is multimodal, considering untreated pain, disease etiology, and environmental and iatrogenic factors, in addition to pharmacologic treatment of psychomotor symptoms.15,68–72

Pain management is a major objective when caring for all critically ill patients. The consistent assessment and treatment of pain in critically ill children may decrease the risk and severity of delirium. This phenomenon may occur partially because of the lessened need for sedatives when a child is already comfortable and calm. A child who is without significant pain is the most likely to maintain a clear sensorium, and often can be comforted by the medical staff and family to relieve anxiety or fear of the strange environment. The goal for an analgesic plan should encourage a multimodal approach73 with heightened use of acetaminophen and nonsteroidal anti-inflammatory agents74 when appropriate, and additional use of opioids to treat severe pain. As with any pharmacotherapy in the PICU, the goal remains the aggressive reevaluation of patients’ specific needs and titration of therapy as soon as appropriate. Use of opioid infusions that are not patient controlled or titrated based on pain-scale scores should be transitioned to longer-acting, intermittent opioids, which may provide a more stable background and decrease the potential for excessive drug administration and, ultimately, sedation. The longer-acting opioid can be enhanced with the intermittent use of shorter-acting opioids to “rescue” the patient from acute uncontrolled pain caused by procedures or other interventions while critically ill. Patients whose clinical course is rapidly changing may benefit the greatest from continuing opioid infusions that are easily titratable. Regardless of the drug or mode of administration, every patient will benefit from consistent reassessment of pain requirements and titration of analgesia, which allow the patient to continue on the road to recovery.75

The PICU environment is unfamiliar and dynamic, frequently demanding the cooperation of patients despite their wishes. The involvement and presence of family, in addition to providing familiar music and filling the room with pictures, toys, and personal items, decreases anxiety and delirium.15,68 Many of the preventive and interventional approaches used for delirium attempt to keep the healthy brain “awake” and decrease the further dysregulation of neurotransmission in the critical care setting. As pediatricians we support the maintenance of daily and bedtime routines in healthy children, which promote a feeling of safety and well-being for a child. In the PICU setting, these routines are challenging to implement owing to monitoring and therapeutic objectives, with the added perception that the child is too sick. A stable environment and day/night routine may be even more important during critical illness.47,69 Children are resilient when provided with the tools to deal with stress, anxiety, and grief, which the medical team in concert with Child Life, hospital teachers, and family can supply.

A preliminary step in the management of patients with delirium is to assess their physiologic status, considering the potential medical causes of delirium. This evaluation should be integrated with an assessment of the environment, recognizing that disruption of the environment will exacerbate misperceptions of thought resulting from delirium. Simultaneously the team must assess the safety of the patient and staff. If safety related to behavioral dysregulation is a concern, pharmacologic intervention should be considered. If, however, safety is not an issue, initial efforts should focus on stabilization of the disease state contributing to the delirium. There are some disease states which, although directly contributing to the onset and persistence of delirium, cannot immediately be reversed. When this occurs, the use of pharmacotherapy to
Patient with COMA (RASS - 4 or - 5)

Delirium assessment cannot be completed at this time because the patient does not respond to voice

Is the patient’s depressed LOC caused by the DISEASE STATE?

YES

ETOIOLOGY

EVALUATE possible causes of Acute Brain Dysfunction (Delirium) → “BRAIN MAPS”

B – Bring OXYGEN (hypoxemia, decreased cardiac output, anemia)
R – Remove or Reduce deliriogenic drugs like anticholinergics, benzodiazepines
A – Atmosphere (foreign room, lights aglowing, noise loud, restraints, absent family, frequent change of caregivers “strangers,” no schedule)
I – Infection, Immobilization, Inflammation
N – New organ dysfunction (CNS, CV, PULM, Hepatic, Renal, Endocrine)
M – Metabolic disturbances (hypo/hypernatremia, hypo/hyperkalemia, hypoglycemia, hypocalemia, alkalosis, acidosis)
A – Awake (No bedtime routine, Sleep-wake cycle disturbance)
P – Pain (too much and not enough drug OR pain treated and now too much drug)
S – Sedation (Assess need and set sedation target)

NO

Depressed LOC caused by SEDATION

1. Establish the TARGET sedation level
   - Set the TARGET LOC at a RASS of 0 (alert and calm)
   - If disease intervention requires a ‘sedate’ patient, Set the TARGET LOC at the most ‘alert’ that will permit needed interventions (e.g., RASS -1, -2, or -3)
   - Discuss the specific benefits of sedation in this patient
2. Provide titration goals to reach or maintain TARGET sedation level
   - Consider less deliriogenic sedatives if depressed TARGET LOC required
   - Titrate or Discontinue use of benzodiazepines if not necessary
3. Follow Pediatric Road Map

PREVENTIVE MEASURES

1. Maintain continuity of care, have loved ones present around the child
2. Create a calm, reassuring environment (comforting pictures, toys, blankets, music, etc.)
3. Establish a day/night routine and periods of uninterrupted rest. Children should be assisted to perform or participate in daily routines of hygiene, mouth care, range of motion exercises, and getting out of bed when awake
4. Consider necessity of tubes, lines, restraints (physical or pharmacologic)
5. Consult child life specialists and/or hospital teachers when appropriate
manage delirium symptoms is indicated for both safety and support of brain function while efforts continue to address the source of critical illness. Patients with persistent delirium, despite initial treatment of the primary disease state, institution of preventive measures, and initiation of antipsychotics to alleviate unwanted effects of delirium, can be disheartening to the team and family. These patients in particular benefit greatly from case presentation during Brain Rounds, because in this setting ongoing discussion of possible causes (BRAIN MAPS) is encouraged, which may lead to a new culprit for the delirium (Box 1). Acute brain dysfunction is not a static process. In the setting of critical illness, aberrant neurotransmission leading to delirium can be cyclic, and caused by new derangements that occur during the patient’s medical course. Critical thinking about delirium among the medical team will increase success in developing the most effective management approach for delirium.

Box 1 summarizes 2 clinical cases highlighted during Brain Rounds in the PICU. Both cases provide examples of how delirium may persist despite pharmacologic treatment of psychomotor symptoms if the source of acute organ dysfunction is not identified and treated. Brain Rounds incorporates the importance of consistently reevaluating possible exacerbating factors for delirium, including new etiologic factors.

It is important to recognize comorbid developmental or psychiatric disorders that may complicate medical management of critically ill children and adolescents. For example, children with autism spectrum disorder have dysregulation when their routine is disrupted. Understanding of the developmental disorder should inform environmental and potentially pharmacologic management of these children. Children with a prior history of trauma may have an increase in dysregulation manifesting as a hyperaroused state (DSM-IV-TR). These children are at risk for increased reactivity in the PICU, which may lead to use of sedatives that complicates the balance of neurotransmitters in the brain. Treatment of their behavioral dysregulation is appropriate; however, the goals of treatment should include understanding of the impact of comorbid disorders on the risk of delirium. Management of the comorbid disorder may result in more beneficial pharmacologic management of delirium.

The management of delirium during critical illness may occasionally require pharmacologic intervention that targets psychomotor behaviors that are harmful to the patient. It must be noted that there is no approval from the Food and Drug Administration for the use of antipsychotics in the treatment of delirium for any age group. Despite this, there is evidence for effective drug therapy in alleviating the symptoms of both adult and pediatric delirium.15,48,70,76 There remains a misperception that treatment with antipsychotics implies psychiatric disorder and that only patients who are psychotic benefit from these medications. Rather, antipsychotics target

Fig. 4. Treatment algorithm for the critically ill pediatric comatose patient. This approach to the management of critically ill comatose patients focuses on how to minimize risks for the development or exacerbation of delirium. This method merges the goals for decreasing risk or severity of delirium with those for management of the critical illness. The outcome is a patient care plan that is mutually beneficial. a This algorithm incorporates the Pediatric Road Map, a method to consistently evaluate pain and anxiety, level of sedation, and delirium. The Pediatric Road Map helps guide discussion during medical rounds to form a multidisciplinary care plan or “map” by answering the following 4 questions: (1) Where is my patient now? (2) How did we get here? (3) Where is my patient expected to go? and (4) How do we get them there? CNS, central nervous system; CV, cardiovascular; LOC, level of consciousness; PULM, pulmonary; RASS, Richmond Agitation-Sedation Scale.
PATIENT AROUSABLE AND DELIRIUM PRESENT (pCAM-ICU+)

Normal OR Depressed LOC + Delirium
HYPOACTIVE DELIRIUM
(RASS 0 to -3 and pCAM-ICU positive)

1. Follow treatment algorithm for Depressed LOC (Fig. 4)
   a. Consider causes of Delirium "BRAIN MAPS"
   b. Consider Preventative Measures
2. Follow Pediatric Road Map
   a. Consider "why" your patient has decreased LOC
   b. Titrate sedation to reach TARGET LOC
3. Consider Psychiatric or PharmD consultation
   a. Consider Atypical Antipsychotics to improve delirium symptoms
      (apathy, withdrawal)
   b. Consider further titration/transition to less deleterious drugs
   c. Consider treatment of Sleep-Wake Disturbances

Critically Elevated LOC + Delirium
HYPERACTIVE DELIRIUM
(RASS +3 or +4 and pCAM-ICU positive)

1. Ensure adequate pain control
2. Ensure patient safety by considering ACUTE sedative administration
   with propofol or benzodiazepines
3. Consider causes of Delirium "BRAIN MAPS"
4. Follow Pediatric Road Map
   a. Reassess and consider "why" patient has agitation
   b. Create plan based on pain score, RASS, and pCAM-ICU
5. Consider Psychiatric or PharmD consultation
   a. Consider transition to Antipsychotics to improve agitation and
      stop long term sedative use which may exacerbate delirium
   b. Consider treatment of Sleep-Wake Disturbances

Mild to Moderate Elevated LOC + Delirium
HYPERACTIVE DELIRIUM
(RASS +1 to +2 and pCAM-ICU positive)

1. Consider causes of Delirium "BRAIN MAPS"
2. Follow Pediatric Road Map
   a. Consider "why" patient has agitation
   b. Create plan to help patient reach TARGET LOC (alert and calm)
   c. Re-evaluate pain score and adequacy of analgesia plan
3. Consider Psychiatric or PharmD consultation
   a. Consider Antipsychotics to improve agitation
   b. Consider treatment of Sleep-Wake Disturbances
4. Consider Preventative Measures (Fig. 4)
neurotransmitter dysregulation, which is clinically present in many diseases of the brain. Delirium is one of those syndromes whereby any level of agitation associated with brain dysfunction may benefit from these medications to restore neurotransmission equilibrium and provide anxiolysis and sedation, enhancing the safety of the child. Lack of understanding in regard of these medications may lead to ineffective use or avoidance of this class of drugs. The decision to use antipsychotics requires careful consideration of the risks and benefits, with the ultimate goal of patient safety.

Haloperidol (Haldol) is the most well-known antipsychotic that is supported for use in the treatment of hyperactive delirium in adults. Haloperidol blocks primarily dopamine receptors in the brain, offsetting overstimulation of higher cortical pathways, alleviating hallucinations if present, providing anxiolysis or sedation, and restoring attention. Haloperidol is a reasonable choice for patients who require intravenous medications and demonstrate agitation that fails to respond to nonpharmacologic interventions.

Atypical antipsychotics, namely risperidone (Risperdal), olanzapine (Zyprexa), and ziprasidone (Geodon) among others, are newer-generation drugs that not only have actions on dopamine activity but also more extensive actions on acetylcholine, serotonin, and norepinephrine receptors. Atypical antipsychotics have been shown in adults to be similarly effective in comparison with haloperidol yet with a relatively low burden of side effects, and future studies in children are required. It has been speculated that patients with hypoactive delirium benefit from atypical antipsychotics such as risperidone because of the modulation of dopamine activity through direct antagonism of the dopamine receptor and indirect antagonism via serotonin receptors, leading to small increases in dopamine activity in key areas of the brain. The effect on multiple receptors helps to reduce the side effects that occur when there is more complete dopamine blockade, as in treatment with haloperidol.

Haloperidol and risperidone have been effectively used in children with delirium without causing significant side effects. Like many other drugs commonly used in the PICU, antipsychotics have side effects that should be considered. Prolonged QTc and extrapyramidal movement disorders, including dystonic reactions, may occur. It is good practice to evaluate and monitor the QTc length in patients who will be receiving haloperidol at baseline and then daily if treatment continues for longer than 24 hours. Dystonic reactions can be easily treated with the use of diphenhydramine and discontinuation of the offending drug. Other cited complications include torsades de pointes, malignant hyperthermia, hypotension, glucose and lipid dysregulation, laryngeal spasm, and anticholinergic effects. As with analgesia or sedation, treatment of delirium also requires reassessment and titration of

Fig. 5. Treatment algorithm for the critically ill pediatric patient with delirium. This approach to the management of critically ill patients with delirium focuses on categorizing the subtype of delirium, patient safety when psychomotor symptoms of delirium are extreme, identifying possible causes, and minimizing exacerbating factors for the development of delirium. The initial steps in management are dependent on the psychomotor behaviors demonstrated by the patient (apathy and lethargy, calm, agitation), which determine the subtype of delirium (hypoactive or hyperactive). The management of delirium relies heavily on critical thinking regarding the possible sources of the acute organ dysfunction, followed by decreasing iatrogenic causes related to the environment or clinical practice, preventive measures, and ultimately the use of pharmacologic interventions to modulate the symptoms of delirium. This algorithm incorporates the Pediatric Road Map (see explanation in the legend of Fig. 4).
the amount of drug once clinical status has improved or side effects such as excess daytime sedation occur. In general, all pharmacotherapy for delirium should be discontinued as soon as the acute phase of organ dysfunction has resolved.\textsuperscript{70}

**SUMMARY**

Monitoring and management of pediatric delirium presents a tremendous opportunity to augment the care of critically ill children. There remain many questions regarding prevalence, risk factors, and outcomes for pediatric delirium, which will be resolved through well-designed prospective pediatric studies. The creation and validation of tools to assist in the diagnosis of delirium among infants and young children will greatly enhance the impact on improving patient care. The lessons learned through the creation and implementation of Brain Rounds, the Pediatric Road Map, and the use of new acronyms for the etiology of delirium (BRAIN MAPS) has provided a consistent mechanism to educate and evaluate the institutional approach to delirium monitoring and management. The reward of the child who survives the PICU and returns to a life of learning, emotional well-being, and future opportunities is worth the considerable effort by the entire medical team in undertaking culture change for delirium monitoring in the PICU.

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**Box 1**

*Delirium management: how Brain Rounds can affect patient care in the critical care unit*

*Patient A* is a 10-year-old boy admitted to the pediatric critical care unit with tick-borne septic shock presenting with symptoms of altered mental status, hypoxia, fever, and hypotension. Other complications in the first 24 hours included metabolic abnormalities (hyponatremia, hypocalcemia, metabolic acidosis, and lactic acidosis) and hematologic complications (anemia, consumptive thrombocytopenia, and leukopenia). The patient was diagnosed with delirium in the setting of ehrlichiosis. Neurology was consulted because of concern for seizure activity, and preventive therapy with levetiracetam was initiated. Despite resolution of the metabolic/electrolyte derangements and aggressive treatment of his tick-borne disease, the patient had persistence of his altered level of consciousness, development of dysregulation of sleep, purposeless movements, and psychomotor agitation 72 hours after presentation. His RASS ranged from +1 to –3. An atypical antipsychotic was initiated to address his sleep disturbance and psychomotor agitation. Brain Rounds promoted discussion of persistent delirium and used BRAIN MAPS to review other possible causes. On further presentation of indolent symptoms of mild respiratory insufficiency and oxygen requirement, and a review of chest radiograph revealing mild cardiomegaly and pulmonary edema, an ECHO was obtained, which revealed severe myocardial dysfunction. The treatment plan included the initiation of cardiac-directed therapies in addition to institution of preventive measures with ongoing pharmacotherapy for restoration of his sleep-wake cycle. Within 48 hours, the patient had resolution of his delirium.

*Patient B* is a teenager who suffered a stroke consequent to rupture of a previously undiagnosed arteriovenous malformation. Following intervention to control intracranial hemorrhage and other related acute neurologic events, the patient suffered from extreme agitation and sleep-wake cycle disturbance during his new steady state. He was diagnosed with delirium and initiated on an antipsychotic, owing to his agitation and dysregulation of sleep. Despite improvement in his psychomotor agitation, the patient continued to demonstrate inattention and frustration with verbal communication. Brain Rounds promoted further discussion on possible causes of delirium and a review of the patient’s psychiatric premorbid history. In addition, with further description of the patient’s agitation there was a realization that he suffered from expressive aphasia, which was likely exacerbating his agitation and sleep disturbance. With the institution of more aggressive occupational therapy and use of creative options for communication, his psychomotor symptoms improved and ultimately the delirium resolved.
REFERENCES


