# Delirium in the NICU: Seeing is Believing or Believing is Seeing?

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Delirium is recognized as a serious condition associated with hospital stays, especially in intensive care units (ICUs) and geriatric settings. Delirium is codified in the American Psychiatric Association's *Diagnostic and Statistical Manual* (DSM-5)[1] and in the World Health Organization's *International Classification of Diseases, Tenth Edition* (ICD-10).

The DSM-5 classifies delirium as a disorder of neurocognition. Symptoms are manifest as acute disturbance in attention, perception, awareness, and changes in cognition, indicating disorganization of thought, such as disorientation, alteration in language, and memory impairment. Other supportive features may be hallucinations or misperceptions, delusions, inappropriate or unsafe behavior, and lability in arousal and emotions, both of which may include hypoactive and hyperactive forms.

By definition, delirium is a syndrome of CNS dysfunction seen as a consequence of another prior medical condition.[2] Examples of such prior, physiologic causes may be from a toxin, disease, injury, medication or other iatrogenic factors. What we "see" is the result of these provocative conditions or events. The "seen" symptoms can be charted explicitly, using validated tools such as the Confusion Assessment Method for the ICU and the Intensive Care Delirium Screen Checklist,[3,4,5] which are considered easy, rapid screens.

These symptom descriptions convey the seriousness of delirium. Delirium diagnoses in adult ICU patients predict longer hospitalizations and subsequent increases in morbidity and mortality. Consequently, the syndrome has become a call for treatment plans and clinical trials for prevention and mitigation. Additionally, with reports of as many as 30 – 80% of patients experiencing hospital delirium (especially in ICUs), investigators have widened their investigations to examine different populations and age groups.[2, 6] Delirium is now reported in pediatric patients, and questions of treatment approaches, including pharmacological interventions are being tested.[5,6,7]

The foregoing summary brings us to the question introduced in the title of this essay: Does delirium arise in the NICU? There is urgency in this question because delirium is a syndrome that creates suffering and, importantly, regularly leads to additional morbidities and even to mortality. Furthermore, delirium is associated with ICU conditions and procedures, many of which prevail in the NICU! (Admission to an ICU or NICU often means separation and isolation; the restraints and stresses of mechanical ventilation are frequently cited as potential iatrogenic precursors, as are the after-effects of some sedatives, etc.).[7-10]

Image by Emanuel Angelicas

Maternal and Infant gaze

There is general acceptance that delirium can be discerned validly and reliably in medical and surgical wards, postoperative recovery areas, emergency departments as well as the ICUs and step-down units. It is reported in geriatric, adult, and pediatric populations. My survey of published reports of delirium in the NICU yielded a small number of case reports.[11,12]

Here, I will bring to the discussion some perspectives and considerations from the field of "developmental science". Though it is not a clinical specialty, I have found that this field has ideas to share with neonatology that are sometimes helpful

in pragmatic ways and often make useful contributions by stimulating fresh approaches and considerations. Let's give it a try.

We'll address two views which can be considered "opposing" perspectives. Admittedly, this is a simplification because each view is contained in the other. Nevertheless, for starters, let's go with the two "opposing" statements: Seeing is Believing and then Believing is Seeing, because an initial separation will help clarify the issues.

I emphasize that I am proceeding with caution and respect because I do not have direct professional experience with hospital delirium. The thoughts that I share here are reactions to the published literature, combined with decades of lab-based experience as a "developmental psychobiologist" working with perinatal animals (rats and mice). Additionally, I am a proud NIDCAP Professional, with approximately 10 years of experience in this specialty within NICUs.

## Seeing is Believing

As officially codified in the DSM-5 and by other respected professional groups, delirium is defined as a syndrome of CNS dysfunction. It is understood as a neurocognitive disorder. What does "neuro" "cognitive" mean in this context? The "neuro" component refers to brain function (dysfunction or encephalopathy in the present discussion). Thus, we consider brain systems as the substrate responsible for the behavioral changes that are manifested. The "cognitive" component refers to some of the non-behavioral changes that contribute to the symptoms. These are changes in thinking, some emotions, perceptions, attention, focus, awareness, and orientation to people and things.

Cognitions themselves cannot be seen: they are inferred and interpreted. Cognitions are usually ascribed to "higher" functions of the mind and brain. As such, cognitive processes are localized in "higher" regions of the brain, particularly the cerebral cortex. Top of the list: Frontal Lobes for "executive functions" such as attention, emotional control, decision making; Broca's Area, in the left frontal gyrus, controlling speech production and word usage; Wernicke's Area, left posterior superior temporal gyrus, understanding meaning of words and sentences, and so on across the cortex where spatial regions cover the interpretation of sensory information as well as many aspects of movements. Together, these areas comprise the core cognitive processes. By observing and questioning a patient, healthcare specialists gather information to assess the status of mental function.

Of the various non-verbal indices of cognition, eye movements are particularly important. Much is known about the functional organization of the visual system, especially the neural controls and cognitive mediators of eye movements. Together, these "neuro" and "cognitive" features provide much of the behavioral and inferred cognitive functions that are interpreted in the standard screening tools for diagnosing delirium in hospital settings. Eye movements that do not fix on faces during interactions suggest social disconnection, eyes that do not track moving objects thus communicate lack of attention or signal disorientation from the present. As a result, Seeing is Believing in the recognition of delirium. The same measures guide choices of pharmacological treatments aimed at treating delirium symptoms. Perhaps not surprisingly, antipsychotic drugs and, more recently, the so-called "atypical" antipsychotic drugs have been the pharmacological treatments of choice for delirium.[9]

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## Believing is Seeing

With a goal of identifying and capturing previously unrecognized cases of delirium, a widening evaluative net is being cast across a variety of hospital units. Consequently, delirium has been discerned in medical and surgical wards, postoperative recovery areas, emergency departments, step-down units, as well as pediatric ICUs[7] Predictably, this net now includes NICUs. At this point, published accounts of delirium in the NICU are limited to a small number of case reports, but the search is underway for the syndrome in NICU populations.[2, 9-12]

Certainly, any syndrome in the NICU that increases morbidities or is developmentally damaging should be identified. But there are reasons to question whether delirium, per se, is a valid diagnosis for newborns, especially those born preterm and who depend on newborn intensive care for weeks or months before reaching 40 weeks (postmenstrual age). There is value in accuracy and in avoiding labelling that can misguide interpretation or deflect focus. This is where developmental science can contribute.

A primary concern is that the current definitions, diagnostic criteria, and tools for defining delirium are based on adult cognition and behavior. A cognitive framework was initially constructed and refined around a syndrome of behavioral

phenomena we call delirium. This cognitive framework was then linked—by inference, not by direct data—to brain dysfunction ("encephalopathy" was an early label), and we have delirium as a neurocognitive disorder! It is said to manifest in pediatric units as with adults in ICUs and elsewhere, and emblematically with geriatric patients. I hasten to add that the Cornell Assessment for Pediatric Delirium (CAPD), a standardized instrument[14] is used, as are other bedside screens. The CAPD is an instrument designed within a cognitive framework. It represents a tacit belief that there are higher-level cognitive processes normally at work in the infant and that these can be provoked into dysfunction. With this belief framework in place, believing can lead to seeing. But is this real, or a kind of illusory 'sleight of hand' trick that we can play on ourselves?

**Gaze has long been used in cleverly designed experiments to reveal infant abilities to detect, discriminate between, and recognize visual stimuli—all perceptual tasks.**

It can be satisfying to see instances of direct continuity from the immature, unformed infant to the mature, differentiated, and integrated adult. But does such "developmental continuity" exist between the diagnosed delirium of children with that of adolescents, adults, and geriatric patients who share a terminologic diagnosis? Accurate, in-depth answers to this question are important because continuities in the disorder would enable tests of common treatments, whereas lack of continuities would immediately challenge the use of common treatments and, importantly, motivate further studies of the syndrome in the infant, adult, and intermediate stages.

Conveniently, the "neuro" side of neurocognition can contribute to this discussion of delirium. Gaze is a great example. Gaze refers to the movements that orient the eyes to a target and fix on it. Gaze has long been used in cleverly designed experiments to reveal infant abilities to detect, discriminate between, and recognize visual stimuli – all perceptual tasks.

But there has been a major shift: the same eye movements are now interpreted as cognitive processes. This has worked pretty well with adult subjects. In delirium, patients often fail to fixate on faces, and their eyes do not track novel objects. They fail to pay attention to people, speech, and their surroundings. Their words and thoughts become similarly disorganized. In adults and children with speech, this spectrum of deficient attention, loss of social connections, and failures of 'executive function' are linked to dysfunction of the cerebral cortex.

We have long known that the cortex is a late-developing structure, displaying multiple forms of immaturity in babies and toddlers and continuing to develop and undergo refinement as long as 20 years in humans! What we have not appreciated until recently is that the cortical control of eye movements and gaze is absent in infants! Yes, the infant's eyes move and can move in a coordinated, functional manner, but the cortex is not yet involved! Instead, it is an alternate, so-called "reflexive" pathway from the eyes and optic nerve directly to the midbrain visual structures, such as the superior colliculus, and directly back to the eye muscles that make the movements. So babies can visually track, fixate, and soon establish and maintain preferential eye contact with parents – but this is accomplished without cortical participation. And remember: we ascribe cognition to the cortex. Thus, gaze in infants does not 'mean' the same thing as it does in adults because infants lack the critical "cortical outflow". This, I must note, is a part of the message contained in the important publication by Blumberg and Adolph[16] that was discussed in a previous issue of the Developmental Observer.[17]

These concerns have important implications for the diagnosis of delirium in the NICU. Gaze by infants can be used appropriately and rigorously for perceptual tests such as detection, discrimination, recognition, or acuity. In contrast, delirium is defined primarily in terms of cognitive function and dysfunction. If we adhere to the established, conventional standard that the late-developing cerebral cortex is the neural seat of cognitive processes, then it is not appropriate to use measures of gaze as an index of cognition in infants, and certainly not for the preterm babies that populate the NICU! In fact, delirium, as it is currently defined, is not an accessible condition, not with the normal scientific standards that are appropriate for applying interventions based on cognitive symptoms!

What should be done? My view—as an initial contribution to a needed dialogue—is that it is vital to have tools to recognize dysfunction in newborns and infants, but the tools, the interventions, and the measures of treatment outcome must be valid, precise, and accurate. Cognitive measures for adults and infants are not comparable. For babies at preterm and corrected infant ages, observational metrics based on Synactive Theory, i.e., autonomic, state, behavior, coupled with systematic evaluations that incorporate normal and necessary procedures, during routine bedside care, examinations, bathing, feeds, and Kangaroo care for example – are sources of valuable

data. In other words, NIDCAP observations[18] (or similar tools from other, related forms of developmental care) offer valid and valuable data for assessments. It is inappropriate, I would argue, to apply to infants batteries of highly interpretive and neurologically counter-indicated methods derived from and developed for adult patients. Words such "disorganized" are more precise and accurate than "delirious", especially when organization/disorganization are described and scored rigorously. Methods such as NIDCAP observations are available, accurate, and preferable.

References


1. American Psychiatric Association. (2013) *Diagnostic and statistical manual of mental disorders, 5th edn* (DSM-5), American Psychiatric Association Publishing
2. Liviskie, C. & McPherson, C. (2021) Delirium in the NICU: Risk or Reality? *Neonatal Network*, 40(2) http://dx.doi.org/10.1891/0730-0832/11-T-727
3. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. (2001) Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med*. May;27(5):859-64. doi: 10.1007/s001340100909. PMID: 11430542..
4. Inouye, S. K., Leo-Summers, L., Zhang, Y., Bogardus, S. T., Leslie, D. L., & Agostini, J. V. (2005). A chart-based method for identification of delirium: Validation compared with inter- viewer ratings using the confusion assessment method: chart Identification of Delirium. *Journal of the American Geriatrics Society*, 53(2), 312–318. https://doi.org/10.1111/j.1532-5415. 2005.53120.
5. Maldonado JR. (2008) Pathoetiological model of delirium: a comprehensive understanding of the neurobiology of delirium and an evidence-based approach to prevention and treatment. *Crit Care Clin*. Oct;24(4):789-856, ix. doi: 10.1016/j.ccc.2008.06.004. PMID: 18929943.
6. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, Truman B, Speroff T, Gautam S, Margolin R, Hart RP, Dittus R. (2001) Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA*. Dec 5;286(21):2703-10. doi: 10.1001/jama.286.21.2703. PMID: 11730446.
7. Mart MF, Pun BT, Pandharipande P, Jackson JC, Ely EW. (2021) ICU Survivorship-The Relationship of Delirium, Sedation, Dementia, and Acquired Weakness. *Crit Care Med*. Aug 1;49(8):1227-1240. doi: 10.1097/CCM.0000000000005125. PMID: 34115639; PMCID: PMC8282752.
8. Wilson, J.E., et al., Ely, E.W. (2020) Delirium, *Nature Reviews/ Disease Primers*, 6:90, https://doi.org/10.1038/ s41572-020-00223-4
9. Adams, S.J. & Sprecher, A. (2022) Delirium in the neonate, *Clinical Perinatology*, 49: 1-14. https://doi.org/10.1016/j.clp.2021.11.001
10. Wilson, J.E., et al., Ely, E.W. (2020) Delirium, *Nature Reviews/ Disease Primers*, 6:90, https://doi.org/10.1038/ s41572-020-00223-4
11. Edwards LE, Hutchison LB, Hornik CD, Smith PB, Cotten CM, Bidegain M. A case of infant delirium in the neonatal intensive care unit. (2017) *J Neonatal Perinatal Med*. 10(1):119-123. https://doi.org/10.3233/NPM-1637
12. Groves A, Traube C, Silver G. (2016) Detection and management of delirium in the neonatal unit: a case series. *Pediatrics*.137(3):e20153369. https://doi.org/10.1542/peds.2015-3369
13. Holberg, M.Y., Larsen, M.H. Mariussen, K.L. & Kyna, N.M. (2021) Delirium in children under two years of age admitted to intensive care units – a systematic review. *Sykepeien Forskning*, 16 (85808) (e85808) DOI: 10.4220/Sykepleienf.2021.85808en
14. Silver, G., Kearney, J., Traube, C., & Hertzig, M. (2015) Delirium screening anchored in child development: The Cornell Assessment for Pediatric Delirium, *Palliative and Supportive Care*, 13(4): 1005-1011. doi:10.1017/S1478951514000947
15. Porter S, Holly C, Echevarria M. (2016) Infants with Delirium: A Primer on Prevention, Recognition, and Management. *Pediatr Nurs*. Sep-Oct;42(5):223-9. PMID: 29406640..
16. Blumberg, M.S. & Adolph, K.E. (2023) Protracted development of motor cortex constrains rich interpretations of infant cognition. *Trends in Cognitive Science*, 2023. 27(3): 233-245. doi.org/10.1016/j.tics.2022.12.014.
17. Alberts, J.R. (2024) Reflecting on motor cortex and its place in developmental care. *Developmental observer,* 17(3): 20-22. DOI: 10.14434/do.v17i3.39755
18. Als H. (1986) A synactive model of neonatal behavioral organization: Framework for the assessment of neurobehavioral development in the premature infant and for the support of infants and parents in the neonatal intensive care environment. *Physical & Occupational Therapy in Pediatrics*. 6(3-4): 3-53.


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