Pain, Delirium or Neuroirritability?

Episodes of Inconsolability in Children with Developmental Delay - Definitions, Evaluation and Treatment

With Drs. Julie Hauer and Stefan Friedrichsdorf

Presentation download of all 3 presentations:
http://NoNeedlessPain.org

A Case

• An 8 year old boy is admitted with 3 hours of screaming
• Diagnosis of adrenoleukodystrophy, failed bone marrow transplant
• No vision, no language, spastic quadriparesis, g tube fed
• Parents feel he is in pain
• He has been doing this long crying jag each evening for a few weeks, but this is longer than most
• No fever, elevated HR, elevated BP
• Is this pain? What is the source? Is this delirium?
• Is this Neuroirritability?

Neuroirritability

• Define irritability
• What is the pathophysiology?
• Model of neuroirritability - infantile colic
• Who is at highest risk?
• Distinguish from delirium
• Clinical evaluation - Dr. Hauer
• Treatment - Dr. Friedrichsdorf

What is Neuroirritability?

• Google and Pubmed search, poll of Child Neurologists
  - Neuro-irritability
  - Neuro-cry
  - Pathologic cry
  - Screaming of unknown origin
  - Central irritability
  - Pain-like behavior
  - Pain or Irritability of Unknown Origin, PIOU
  - Irritable insomnia
  - Light-Switch mental status change
  - Paroxysmal fussiness

Crying is Communication

• Crying as part of a communication loop
• Nonverbal expression of need
• Caregiver physiologic response - increased heart rate, endocrine changes
• Caregiver tries to interpret and to meet the child’s need
• Successful interaction encourages communication, provides feedback to caregiver - solidifies bond
Crying differs in neurologic impairment

• f0- frequency of cry: speed of opening and closing of the vocal cords
• Typical f0 is 350-700 Hz, abnormal is 1000-2000 Hz
• Higher f0 cries in prematurity, brain injury, chromosome abnormality
• Autism spectrum often have few facial expression changes and cry modulation seen as atypical
• Higher f0 cry, atypical cry pattern is perceived as more aversive, distressing
• Inability to soothe leads to risk of caregiver distress

Crying is not the only sign of distress

• Facial features: grimace
• Change in sleep pattern: increase or decrease
• Increase in abnormal movements: more spasticity, dystonia, stereotypy
• Decrease in movements: freezing
• Autonomic changes: HR, sweating, flushing
• Self harm: biting, scratching, head banging
• Atypical or idiosyncratic reactions: laughing

Pathophysiology of Neuroirritability

• Abnormal cognitive, communication and motor systems
• Is it pain?
  – This population at high risk for pain (musculoskeletal, skin, GI, dental, headache, colostomy)
  – Oversensitized to pain: From prior painful stimuli (gut dysmotility, GERD and constipation, hydrocephalus, surgeries)
  – Excessive response to mild discomfort: Hyperalgesia
  – Pain response to typically nonpainful stimuli: allodynia
• Is it emotional?
  – Overstimulation by the environment
  – Autistic patients: Specific anxiety treatment often effective
  – More rapidly cycling irritability: seen in patients with developmental delay and family history of bipolar disorder
  – Caregiver distress: sometimes neuroirritable behavior varies with provider; cause or effect?

Pain Systems

• Nociceptive
  – Normal response to tissue damage
• Neuropathic
  – Pain due to lesion or disease of the Peripheral or Central Nervous system
  – Genetic or acquired
  – Abnormal pain signals without ongoing injury
  – Hyperalgesia, allodynia

Infantile Colic- Normal Neuroirritability?

• Paroxysmal fussiness in infancy
• Irritable, cry, arch back, twist trunk, extend legs
• Typically starts after 2 weeks of age, decreases by 3-4 months
• > than 3 hrs of crying, >3 days per week, for > 3 weeks in an infant
• Inconsolable
• Higher risk of poor bonding, of caregiver frustration, of abuse
• Immature nervous system?- processing the sensory input of the day
• Hyper-reactive or hyper-sensitive child
• Higher association with anxious parents- direction of causality?
• Query gut pain? Though typical GI treatments (reflux, gas) not shown to impact this behavior
• Predictor of Pediatric Migraine

Colic- Infant Migraine or Marker of Genetic Risk
• Mothers with migraine 2x more likely to have infant with colic
• Infantile colic raises likelihood of migraine, OR 5.6
• Is it an infant migraine? Or sign of an abnormal nociceptive system?

Pediatric Migraine- Neuropathic pain?
• Pediatric Migraine triad
  – tendency to motion sickness
  – tendency to ice-cream headaches
  – suffer from growing pains
• Overzealous pain reaction to simple stimuli
  – dehydration
  – skipped meals
  – poor sleep
  – hormonal changes
  – environmental changes- loud sounds bright light

An oversensitive brain?
• Colic as a model of developmentally typical Neuroirritability
  – Immature brain, based on a genetic tendency, associated with neuropathic pain syndrome
• Neuroirritability in Severe Neurologic impairment
  – A normal or excessive response to nociceptive pain?
  and/or
  – Pathological response to other non-pain stimuli?

Who is at risk of Neuroirritability
• Any child with severe neurologic impairment- cognitive, communication, motor impairments
• More severe at higher risk
• Especially those with dynamic CNS changes- neurodegeneration, inflammation, intractable seizures
• May depend also on underlying genetic tendency to neuropathic pain
• May depend also on mood and environmental issues

• Degenerative neurologic disease- adrenoleukodystrophy, mucopolysaccharidosis, Krabbe
• Acute brain injury- hypoxic ischemic injury, trauma, kernicterus
• Inflammatory brain disease- NMDA-R encephalitis, opsoclonus-myoclonus-ataxia, infectious encephalitis
• Metabolic disease- mitochondrial disease, amino acidopathies
• Chromosomal abnormalities- cri du chat (5p-), other
• Severe impairment, subset of these patients- epileptic encephalopathy, quadriplegic cerebral palsy, autism with intellectual disability
Neuroirritability or Delirium?

- **Delirium**
  - Acute onset change in mental status
  - Fluctuations
  - Inattention or confusion
  - May have other symptoms - hallucinations, change in sleep wake cycle, autonomic instability

- Caused by acute disruption of brain centers controlling attention, arousal, memory
  - Seizure, infection, new focal injury, metabolic derangement

- Any seriously ill patient is at risk of delirium
- Patients with severe neurologic impairment at high risk, difficult to assess
- May depend on context - is the patient ill? have there been acute neurologic changes?
- Neuroirritability often more prolonged, more chronic

Medical Evaluation in Neuroirritability

- Clinical diagnosis, not a diagnosis of exhaustive exclusion
- Take into context - parental report, relationship to feeding, evacuation, moving, environmental changes, medications
- Good examination - teeth, ears, skin, diaper area, belly, bones
- Neurologic status - worsened movement disorder, seizure
- Lab workup - infectious, inflammatory
- Imaging - brain, belly, bones

Treatment of Neuroirritability

- Siden et al. - PUP, Pathways for Unknown Pain
  - Standard analgesics
  - Gabapentin, other antiepileptics
  - Antispasmodics
  - Antihistamines, Benzodiazepines
  - Opioids
- Nonpharmacologic interventions
  - Diaper change, vent g tube, change position
  - Decrease environmental stimulation
  - Music, massage, other sensory treatments

- Thank you!
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References: