Procedural pain and distress in children: What you do not know may harm them!

Gary A. Walco, PhD, ABPP
Professor of Anesthesiology, (adj.) Pediatrics and Psychiatry
University of Washington School of Medicine
Director of Pain Medicine
Seattle Children’s Hospital

April 22, 2016
California Society of Pediatric Dentistry
Western Society of Pediatric Dentistry
Disclosures

- Consultation to Pfizer Pharmaceuticals
- Special Government Employee, United States Food and Drug Administration, Anesthetic and Analgesic Drugs Products Advisory Committee
- Chair, Pediatric Research Network for Pain (PRN-Pain), Co-Chair Pediatric Pain Research Consortium and member of executive committee, Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION)
- Contributor to UpToDate
A little procedural distress humor…

"We’re all out of Novocain, so we need to restrain your arms and legs."

“What’ll it be—Novocain or Yanni?”

Seattle Children’s
HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
SCHOOL OF MEDICINE
René Descartes (March 31, 1596 – February 11, 1650)
Descartes’ contributions (partial list)

- Mathematics: Cartesian Geometry
- Medicine: Reflex theory
- Philosophy: Skepticism and rationality—Cogito ergo sum
- Psychology: Analysis of primary emotions
Les passions de l’ame (Passions of the Soul) 1

- 1649
- Most extensive account of mind-body interactions
- Intersection of soul and body at the pineal gland
Descartes’ quotable quotes

• “It is not enough to have a good mind. The main thing is to use it well.”

• “If you would be a real seeker after truth, you must at least once in your life doubt, as far as possible, all things.”

• “Omnia apud me mathematica fiunt.” (With me everything turns to mathematics.)
Descartes’ model of pain (1664)*

A number of sources cite the date of publication at 1664. Descartes died in 1650. Never complain to your journal editors about turnaround time for production.
The pineal gland is here
Cartesian dualism: Separation of mind and body

- **Peripheral models**
  - emphasis on physiological factors
  - “real” pain

- **Central models**
  - emphasis on psychological factors
  - “It’s all in your head” pain

- **Holistic models**
  - emphasis on the integration or unification of physiological and psychological factors
One may think that in the ideal world….
In the real world

- Goal: Prevent and treat behavioral distress
- Synergistic sum of pain + anxiety
- These elements are inseparable
How do we know someone is in distress?

• Self-report of subjective internal state
• Behavioral observations
• Physiological indicators

• Do they match up?
• Which do we believe?
• Which is most important to treat?
How do these indicators correlate?

- Children with cancer 3.1 to 17.7 years of age undergoing lumbar puncture
- Self report (anxiety, anticipated pain, and others)
- Parent report (own and child’s anxiety)
- Behavioral observations (Procedure Behavior Checklist)
- Physiological indicators (heart rate, vagal tone, salivary cortisol)

How do these indicators match up?

- Among the correlations between self-report and behavioral observations, only parent ratings of child anxiety and the total behavior score prior to the procedure were significantly related ($r = 0.39$, $p = 0.048$).
- Values were very low in correlating total behavior scores with salivary cortisol (pre-procedure, $r = -0.14$; behavior during and post-procedure with second cortisol levels, $r = 0.00$ and $r = -0.15$, respectively, all $p > 0.05$).
- Similar results were obtained in evaluating the relationship between distress behavior and both heart rate and cardiac vagal tone.

Main regions activated in response to acute nociceptive stimulation (see diagram on right):

- Spinal cord
- Thalamus
- S1 and S2
- Insula (not always same division)
- Anterior cingulate cortex (not always same division)
- Prefrontal cortex

**BUT THEN ALSO perhaps:**

- Amygdala
- Hippocampus
- Posterior parietal cortex
- Basal ganglia
- Brainstem

fMRI: Neuroanatomy of stress and anxiety responses

- **Stress**
  - ↓ activity of orbitofrontal regions
  - ↑ activity in frontal lobes, especially anterior cingulate cortex
  - ↓ activity of limbic system, especially hippocampus

- **Anxiety**
  - ↑ activity amygdala
  - ↑ activity dorsal anterior cingulate cortex
  - ↓ activity in ventromedial prefrontal cortex including the subgenual anterior cingulate cortex and the medial orbitofrontal cortex

Neurotransmitters: chronic pain

# Neurotransmitters: depression and anxiety

**Depression**
- Serotonin
- Norepinephrine
- Dopamine
- Inflammatory cytokines

**Anxiety**
- Serotonin
- Norepinephrine
- GABA
- Corticotropin-releasing factor (CRF)
- Glutamatergic system
- Neuropeptides: substance P, neuropeptide Y, oxytocin, orexin, and galanin
The long-term sequelae of poorly treated pain

- **Physiological**
  - Increased nerve growth factor and sprouting
    - ↑ differentiation ↓ integration
  - Central sensitization
- **Psychological**
  - Conditioned aversions
  - Trauma
- **Stress responses and pain**
Infant vs. adult acute pain processing

• Psychobiological effects of overwhelming stress (chronic, focal and acute)
• Limbic-hypothalamic-pituitary-adrenal (LHPA) axis and the locus coeruleus-norepinephrine/sympathetic nervous system, catecholamine system
• Early traumatic experiences and related elevations in corticotrophin releasing factor impact long-term dysregulation of the LHPA system, causing sensitization to future stressors
• The neurotransmitter system, highlighting the roles of serotonin, norepinephrine, and dopamine, as well as other neuroendocrine and autonomic responses, are key, with many systems clearly paralleling those involved in central sensitization associated with chronic pain syndromes
Managing procedural distress

- Optimal strategies address
  - Nociceptive stimulation
  - Anxiety or stress
- Specific strategies invoked depend upon the nature of the procedure and the individual person involved
  - Invasiveness of procedure
  - Developmental concerns
  - Individual differences
    - Temperament and personality
    - Coping styles
      - Attenders
      - Distractors
Distractors
Parental coping
### Adult behaviors

<table>
<thead>
<tr>
<th>Things that make it <strong>worse:</strong></th>
<th>Things that help:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Criticism</td>
<td>• Non-procedural talk (distraction)</td>
</tr>
<tr>
<td>• Reassurance</td>
<td>• Humor</td>
</tr>
<tr>
<td>• Apologies</td>
<td>• Suggestions on how to cope</td>
</tr>
<tr>
<td>• Empathy</td>
<td>• Giving appropriate control</td>
</tr>
<tr>
<td>• Giving inappropriate control</td>
<td></td>
</tr>
<tr>
<td>• Threats</td>
<td></td>
</tr>
</tbody>
</table>

An ethical question?

- Pediatric care providers are committed ethically and morally to doing no harm to their patients.

- **Exposing child to pain that is treatable**, especially if there may be long-term deleterious effects of that pain, is inconsistent with the “do no harm” doctrine, and therefore is unethical.

- How much pain or distress is generated by a given insult or pathological condition is not up to the care provider, but resides with the patient.

- Young children, in particular, consider needle pain to be “clinically significant”.

- Recent data show long-term physiological and psychological impact of under- or un-treated pain in the young.

A public health issue

- Population: 36% dental anxiety; 12% extreme dental fear
- Comprehensive literature review focused on causes and consequences
  - Exogenous factors
    - Direct learning from traumatic experiences
      - 61% of adults, 50% of whom acquired in childhood
      - Injection of local anesthesia
      - Sexual assault victims 2.5X more likely
    - Vicarious learning through significant others and the media
      - Parent-child correlations
      - Sibling experiences

A public health issue

- Endogenous factors
  - Inheritance
    - Twin studies (females > males)
  - Personality traits
    - Neuroticism (anxiety, self-consciousness, hostility and depressive symptoms)
    - Extraversion (warmth, excitement seeking and assertiveness)
  - Cognitive ability
    - Among children, ↑ IQ associated with ↓ dental fear

A maladaptive cycle

Thank you for your attention