Effects of Anesthesia on Pediatric Brain MR Imaging

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Anesthesia and MRI

• Pediatric MRI highly dependent on anesthesia
  – All young children (<6 years)
  – Some older children (behavioral, respiratory issues, apprehension)
  – Orbit imaging
  – ~50% of MRI in our pediatric practice
Anesthetic Physiology

• Anesthesia has known effects on
  – Cerebral blood flow (CBF) and cerebral blood volume (CBV)
  – Vasoreactivity and vessel caliber
  – Cerebral metabolism
  – Normal neurovascular coupling
Physiologic & Anatomic MR Imaging

- Anesthetic effects may manifest in many ways on MRI
  - Cerebral blood flow (CBF) and cerebral blood volume (CBV)
    - Perfusion MRI
  - Vasoreactivity and vessel caliber
    - Perfusion MRI
    - Susceptibility-weighted imaging
    - fMRI
  - Cerebral metabolism
    - Perfusion MRI
    - fMRI
  - Neurovascular coupling
    - fMRI
  - CSF Artifact
    - FLAIR imaging
Intravenous Anesthetics/Analgesics

- Examples:
  - Propofol
  - Etomidate
  - Thiopental
  - Midazolam
  - Diazepam
  - Fentanyl
  - Dexmedetomidine
  - Sufentanil

- Most decrease cerebral metabolism
- Decrease CBF
  - Vasoconstriction
  - Inhibition of NO-mediated vasodilatation
  - Secondary to decrease in cerebral metabolism
- Depress EEG response (cortical activity)
  - Prototype: propofol

Inhalational Anesthetics

- Increase cerebral metabolism
- Effect on CBF varies with time and dose
  - Initial increase, then decrease
  - Direct vasodilators (increases with dose), independent of CMR
- Decoupling of CBF and cerebral metabolism
- Frequently used with another agent (ex: propofol)

Examples:
- Sevoflurane
- Desflurane
- Isoflurane
- Enflurane
- Halothane
Perfusion effects differ

- DSC perfusion MRI in 55 children
- CBF did not follow expected age-related curve in anesthetized patients
- Age-related trends in CBF, CBV differed between anesthesia types

- Anesthesia-induced changes in perfusion could be mistakenly attributed to pathology
  - Ex: comparison or longitudinal analysis of global perfusion changes due to therapy or disease

What about ratios?

• Ratio-based measures of CBV, CBF used to grade tumors, distinguish from radiation necrosis
  – Tumor: normal brain
    • rCBV > 1.98, rCBF > 1.25 = high-grade glioma (Hayyemez et al, 2005)
  – Lesion: normal brain
    • rCBV > 2.1 = recurrence (vs. radiation necrosis) (Mitsuya et al, 2010)
    • rCBV > 1.75 predicts progression (Law et al, 2006 & 2008)
Ratios

• Tumor: normal brain ratio may change with anesthesia
  – Vasoreactivity of tumor neovascularity likely differs from normal vessels

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<thead>
<tr>
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<th>Normocapnia</th>
<th>Hypocapnia</th>
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<tbody>
<tr>
<td>Isoflurane</td>
<td>3.2</td>
<td>3</td>
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<tr>
<td>Propofol</td>
<td>4.3</td>
<td>3.1</td>
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Adapted from Cenic et al, 2005

• GM:WM ratio
  – Generally accepted that CBF and GM/WM ratios decrease with age (Huisman 2004; Biagi 2007; Ogawa 1989)
  – Trends altered with anesthesia

Awwad, Harreld et al, ISMRM 2013
Vessel conspicuity on SWI

- Veins appear dark on SWI due to deoxyhemoglobin
- Increasing CBF, ETCO$_2$ decreases venous deoxy-Hb (more oxygenated venous blood), decreasing venous conspicuity [BOLD effect] (Sedlacik et al, 2010)
  - Could lead to underestimation of extent of vascular lesions (ex: AVM)
  - Could impact attempts to stage tumors with SWI (Hori et al, 2010)

Sevoflurane.
CBF=78.9, CBV=10.5, ETCO$_2$=51

Propofol.
CBF=40.9, CBV=5.65, ETCO$_2$=37.25
CSF Artifact on FLAIR

- Artifactual CSF signal intensity in sulci and cisterns can mimic or obscure leptomeningeal disease
- Attributed variably to
  - Anesthetic agents
  - Supplemental O₂ administered with anesthesia
    - Attributed to T1 effects
  - Recent study found effect of anesthetic agent to be dominant (Harreld et al, ASNR 2012)

Variable sulcal signal intensity in patients without leptomeningeal disease.
CSF Hyperintensity on FLAIR–Artifact or Disease?

6yo M with L frontoparietal skull Ewing sarcoma. Post-contrast FLAIR image (left) [3T; TR10000, TE 108, TI 2604.7, 20 ch head coil] shows diffusely increased signal in sulci.

Scan 1. Increased signal in sulci.

Scan 2. Increased signal in sulci has decreased.

Same patient 3.5 months later, no intervening treatment. Same magnet and imaging parameters. Post-contrast FLAIR image (left) shows decrease in increased signal in sulci. Only difference: Sevoflurane GA on Scan 1 (see oral airway device) and propofol on Scan 2 (see NC).
fMRI

- **Neurovascular coupling**
  - Neurons
  - Astrocytes
    - **Coupling** of post-synaptic activity to **metabolism** and vascular response (CBF)
  - Vessels

Relatively less extraction $O_2$, so MORE $O_2$-Hb (paramagnetic), in that volume of blood

↑Signal in activated volume (↓% paramagnetic Deoxy-Hb, which ↓signal)

**BOLD EFFECT**
Anesthetic Actions on Neurovascular Coupling

1. Optimal Stimulus Frequency
   - ↓ Isoflurane

2. Latency
   - ↑ Propofol
   - ↑ Isoflurane (dose-related)
   - Δ Ketamine, fentanyl

3. Neuronal Activity
   - GABA-ergic:
     - ↓↓ Propofol
     - ↓↓ Pentobarbital
     - ↓ Isoflurane

4. Glutamatergic transmission
   - ↓ Ketamine, pentobarbital

5. CBF
   - ↓ propofol, fentanyl, diazepam, midazolam
   - ↑ isoflurane, sevoflurane

6. Cerebral Metabolism
   - ↓ propofol, fentanyl, diazepam, midazolam
   - ↑ isoflurane, sevoflurane
   - ↑↑ halothane

7. CBF-Metabolic Coupling
   - ↓ volatile anesthetics (thanes)

8. Spatial Coordination
   - ↓ Isoflurane

References:
fMRI

• Propofol (and other IV anesthetics) decrease cortical activity and CBF
  – CBF response (coupling)
    • preserved at sedative, but not hypnotic, concentrations (Veselis 2005)
  – Latency
    • increases with propofol (Franceshini 2010)
• Volatile anesthetics (e.g. sevoflurane, isoflurane)
  – Disrupt CBF-Metabolic coupling
  – May affect optimal stimulus frequency
  – May alter spatial coordination of activation and BOLD signal
Conclusion

- Significant challenge in pediatric neuroimaging
- Be cautious when interpreting quantitative MR imaging in anesthetized children
- Be aware of effects on anatomic images (FLAIR, SWI)
- Possible solutions
  - Standardized anesthesia
  - New “normals” for CBF, CBV under anesthesia
  - Consideration in statistical analysis
  - More research characterizing effects in children
    - More sensitive than adults to vasodilatory effects sevoflurane
    - Data in adults may not apply to children


