

Anesthetic toxicity in the pediatric brain

Greg Stratmann, UCSF

876 • The Journal of Neuroscience, February 1, 2006 • 26(3):876–882

Early Exposure to Common Anesthetic Agents Causes Widespread Neurodegeneration in the Developing Rat Brain and Persistent Learning Deficits

Yessna Jevtovic-Todorovic,¹ Richard E. Hartman,² Yukitoshi Izumi,¹ Nicholas D. Benschoff,² Krikor Dikranian,¹ Charles F. Zorumski,¹ John W. Olney,² and David F. Wozniak¹
¹Department of Anesthesiology, University of Virginia Health System, Charlottesville, Virginia 22908, and Departments of ²Neurology and ³Psychiatry, Washington University School of Medicine, St. Louis, Missouri 63110



The NEW ENGLAND
JOURNAL of MEDICINE

HOME | ARTICLES | ISSUES | SPECIALTIES & TOPICS | FOR AUTHORS

Perspective

Defining Safe Use of Anesthesia in Children

By: Rappaport, M.D., R. Daniel Melton, Ph.D., Arthur Simone, M.D., Ph.D., and Janel Woodcock, M.D.
March 9, 2011 (10.1056/NEJmp1102155)

The New York Times

Science

WORLD | U.S. | NY / REGION | BUSINESS | TECHNOLOGY | SCIENCE | HEALTH | SPORTS | OPINION | ENVIRONMENT | SPACE & COSMOS

F.D.A. to Study Whether Anesthesia Poses Cognitive Risks in Young Children

By: PAUL BELLUCK
Published: March 9, 2011



Outline

- Does it happen in humans?
- Implications for my practice

Does it happen in humans?

- Yes (maybe): Wilder, Kalkman, DiMaggio, Di Maggio
- No: Sprung, Hansen, Bartels, DiMaggio

Outline

- Does it happen in humans?
- Implications for my practice

Outline

- Does it happen in humans?
- Implications for my practice

Implications for my practice

- Human literature controversial. Animal literature clearer. What to believe?
- Scepticism far more comfortable than credulity
- Why wouldn't anesthesia cause ill effects in infants? (Nature, nurture)

Hypothesis

- Environmental enrichment rescues function.

Methods

P7 male Sprague Dawley rats (n=100)

Control (n=50)
4h maternal separation,
FIO₂=0.5

Sevoflurane (n=50)
4h, 1 MAC (**Clamp 50%**)
FIO₂=0.5

3 weeks (P28)

Regular housing
(n=17)

Environmental
Enrichment (n=18)

Regular housing
(n=20)

Environmental
Enrichment (n=18)

5 weeks (P63)

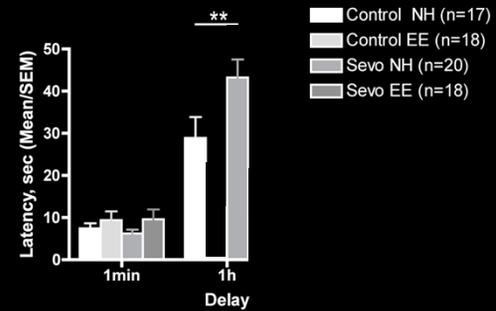
Fear conditioning, Working memory, Short term memory, Long term memory



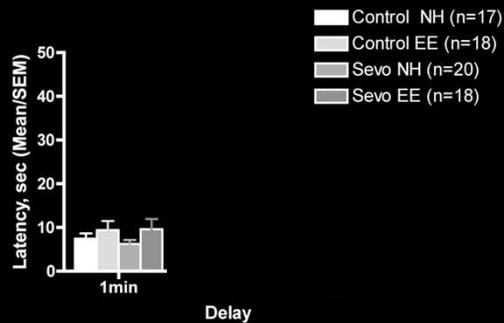
Results

- Sevoflurane impairs spatial short term memory.
- Environmental enrichment rescues function.

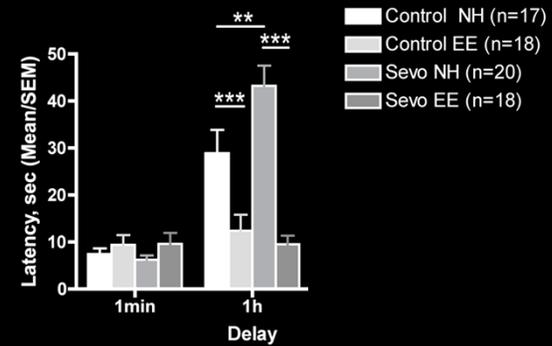
Sevoflurane Causes Spatial Short Term Memory Deficit



Sevoflurane Causes Spatial Short Term Memory Deficit



Sevoflurane Causes Spatial Short Term Memory Deficit
Delayed Environmental Enrichment Rescues Function



Conclusion

- In rats, anesthesia-induced neurocognitive dysfunction is treatable.
- In rats, a lifestyle change long after anesthesia trumps anesthetic exposure.

Results

- Sevoflurane impairs spatial working memory.
- Environmental enrichment rescues function.
- Tissue trauma adds nothing to anesthesia-induced deficit.

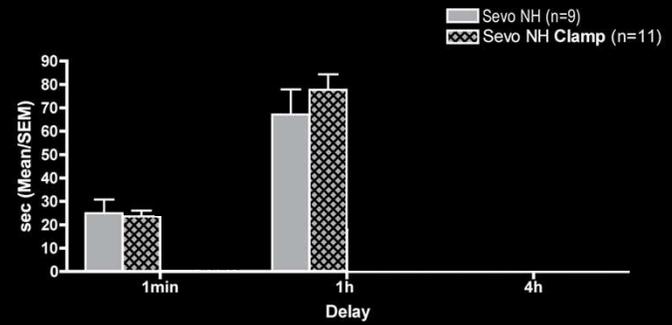
Implications for your practice - some quotes

- “Surgery might be the problem, not anesthesia”
- “Don’t waste time under anesthesia” (What duration of anesthesia is safe?)
- “Delay elective surgery if possible” (Until when? What is the vulnerable period?)
- “Do not use mixed agents” (Equipotency)
- “Avoid multiple anesthetics”

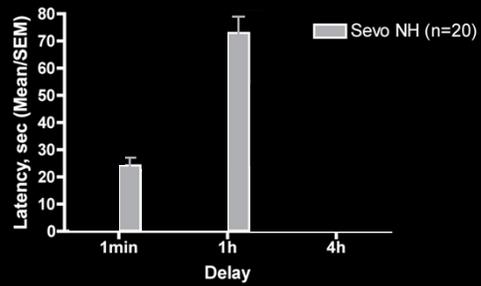




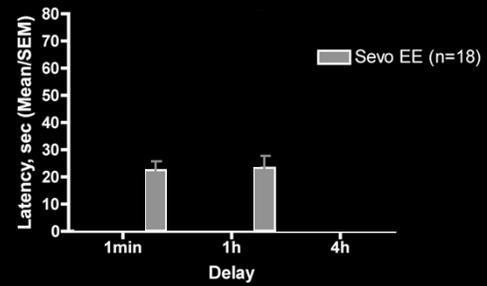
Tissue trauma adds nothing to anesthesia-induced deficit.



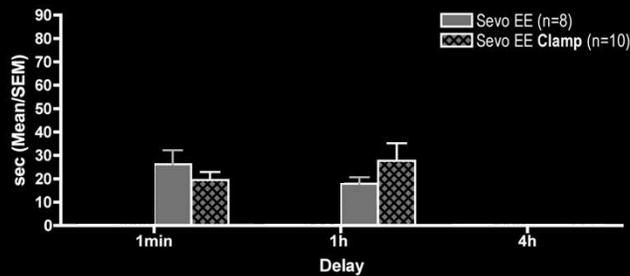
Tissue trauma adds nothing to anesthesia-induced deficit.



Tissue trauma adds nothing to anesthesia-induced deficit.



Tissue trauma adds nothing to anesthesia-induced deficit.



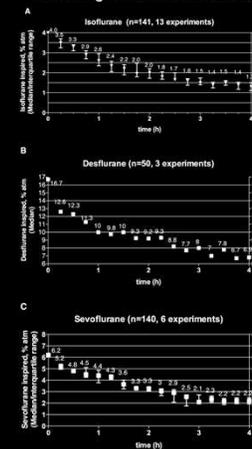
Implications for your practice- Unanswered questions

- Does it happen in humans? (Smart Tots, Panda, GAS)
- Can it be prevented?
- Can it be treated?
- What is the safest anesthetic?

Implications for your practice - some quotes

- “Surgery might be the problem, not anesthesia”
- “Don’t waste time under anesthesia” (What duration of anesthesia is safe?)
- “Delay elective surgery if possible” (Until when? What is the vulnerable period?)
- “Do not use mixed agents” (Equipotency)
- “Avoid multiple anesthetics”

In Immature Rats, MAC of Volatile Agents Decreases With Increasing Duration of Anesthesia



Outline

- Does it happen in humans?
- Implications for my practice

Thank you!

stratman@anesthesia.ucsf.edu

Acknowledgements

Stratmann Lab

- Tatiana Ramage
- Flora Chang
- Jen Shih
- Rehan Alvi
- Alison Rowe
- Gopal Lalchandani
- Marianna Yusupova
- Heidi Gonzalez
- Laura May
- Jason Shieh
- David Lempert
- Dana Ben Tzur
- Kyle Barbour

In-House Collaborators

- Jeff Sall
- Ted Eger

Behavioral Neuroscientists

- Simona Ghetti (UC Davis)
- Howard Eichenbaum (Boston U)
- Andy Yonelinas (UC Davis)

Funding Agencies

- APSF, FAER, IARS

UCSF, Department of Anesthesia

What I really think

Anesthesia Impairs Recollection in Humans

