

annual report
2015

SmartTots



IARS

International Anesthesia Research Society

Improving Health through Discovery and Education

about us



The SmartTots program is a multi-year collaborative effort designed to increase the safety of anesthetic and sedative drugs for the millions of children who undergo anesthesia and sedation each year.

To address the growing concern about the potential adverse consequences of general anesthesia in young patients, in 2009 the U.S. Food and Drug Administration (FDA) established a public-private partnership with the International Anesthesia Research Society (IARS). The partnership is working together with multiple stakeholders, including academic research institutions, medical professionals and societies, and other government and nonprofit organizations to address scientific and clinical gaps regarding the safe use of anesthetics and sedatives in children. While non-human studies confirm a link between anesthesia use and damage to the developing brain in animals, currently there is insufficient clinical evidence to determine whether a clear link exists between the effects of these drugs and the development of the human brain. SmartTots is working to address the gaps in research and make anesthesia and sedation safer for children around the world. The following annual report delineates SmartTots successes during 2015.

On behalf of the SmartTots Steering Committee and its Scientific Advisory Board, it has been our privilege to steward your donations this past fiscal year toward our collective goal of making anesthesia safer for children.



2015 Research Milestones

SmartTots had a key role in the important progress that was made in pediatric anesthesia research during 2015.

We contributed to the advancement in research by funding these significant studies:

Lena Sun, MD

Columbia University Medical Center, New York, New York

Pediatric Anesthesia NeuroDevelopment Assessment (PANDA) Study

The purpose of this study, begun in 2009 using ambidirectional cohort design, is to determine whether the use of anesthetic agents in infants and children have long term adverse effects on neurocognitive development. During 2015, Dr. Sun conducted the final stages of her research, reporting that she successfully analyzed 116 sibling pair participants. She also obtained 23 completed anesthesia records in the exposed cohort to analyze whether low-flow versus high-flow sevoflurane anesthesia (based on fresh gas flow relative to minute ventilation) is associated with differences in results of neurocognitive testing. It is anticipated that the study will be complete and results reported by June 2016.



Jeffrey Sall, PhD, MD

University of California San Francisco, San Francisco, CA

Recognition Memory Following Early Childhood Anesthesia

Dr. Sall originally received SmartTots funding in 2013. His research examines the limits or boundary conditions of early childhood anesthesia exposure that may lead to cognitive deficits. His project will determine how the duration of anesthesia exposure and the age of the child at the time of exposure affect recognition memory deficits.

During 2015, the study was more than 50% complete and continuing to make progress, actively partnering with academic centers around the country to recruit and test subjects. Once complete, the results will provide guidance to clinicians and parents when deciding to perform certain procedures and will give future researchers an important outcome measure that is easily testable.



2015 Research Milestones

Robert Block, PhD

University of Iowa, Iowa City, Iowa

General Anesthesia During Human Infancy and Brain Development

Originally funded by SmartTots in 2012, Dr. Block aimed to evaluate the hypothesis that exposure to general anesthesia and surgery during infancy affects brain and cognitive development as reflected in measures of brain tissue volume and composition and white matter integrity, memory-related regional brain activation, and cognitive test performance. By 2014, Dr. Block's study analysis found that there were lower white matter volumes and diminished white matter integrity in patients, relative to controls. He also reported finding some differences in brain activity associated with long-term memory and working memory processes in patients, relative to controls. Dr. Block intends to complete the analyses of the present study, publish the results, and seek funding from NIH for a substantially larger-scale study to replicate and extend the results. His new research would involve studying more patients with a broader age range of exposure to anesthesia and comparing patients who were exposed for more vs. less invasive procedures, in addition to unexposed controls.



Caleb Ing, MD

Columbia University Medical Center, New York, New York

Anesthetic Exposure Duration and Effects on Cognitive and Language Ability

Also funded in 2012, Dr. Ing and colleagues began conducting research to determine the relationship between anesthetic exposure before the age of three and long-term neurodevelopmental deficits using a battery of directly administered neuropsychological assessments. As of March 2015, Dr. Ing and team reported two important research findings, they found that in their cohort, the determination of neurodevelopmental deficit depended on the outcome used, with differences in children exposed to anesthesia found using neuropsychological outcome measures and clinical diagnoses but not with academic achievement tests. His team was also able to determine that initial exposure to anesthesia after age 3 had no measurable effects on language and abstract reasoning, suggesting that there may be distinct windows of vulnerability for different neurodevelopmental domains in children.



2015 Research Milestones

During late 2015, researchers announced the secondary outcomes from the first, randomized anesthesia trial in kids.

Recent Study Shows No Difference between General Anesthesia and Regional Anesthesia in Short Duration Surgery, October 2015

General Anesthesia Compared to Spinal Anesthesia (GAS) study researchers release report describing the secondary outcome of cognitive performance at 2 years of age based on 532 subjects. [Read more](#)



SmartTots released an updated Consensus Statement


The growing body of evidence from animal studies and observational studies in humans continues to suggest adverse effects on behavior, learning, and memory may result from exposure to anesthetics and sedation during periods of rapid brain development. The International Anesthesia Research Society and US Food and Drug Administration reconvened a group of experts in anesthesia, pediatric medicine, neuroscience, and patient safety to consider the additional evidence and what it means for health care providers and parents.

The 2015 SmartTots **Consensus Statement on the Use of Anesthetic and Sedative Drugs in Infants and Toddlers** is the result of many hours of deliberation by that diverse group of experts. The newly updated Consensus Statement is endorsed by the FDA, the IARS and 17 additional stakeholder organizations. [Read more](#)

SmartTots Urges Continued Research on Possible Effects of Anesthesia on Young Children; Issues Supplement to Recent Consensus Statement

During November, immediately following the announcement of the secondary outcomes from the clinical trial, General Anesthesia Compared to Spinal Anesthesia (the GAS Study), SmartTots once again convened more than 30 experts in anesthesia, pediatric medicine and neuroscience to discuss the trial's early findings and consider their significance.

The Consensus Statement Supplement was developed as a result of this meeting. [Read more](#)




Consensus Statement on the Use of Anesthetic and Sedative Drugs in Infants and Toddlers October 2015

Each year, millions of infants and toddlers require anesthesia and/or sedation for surgery, procedures, and tests. Concern has been raised about the safety of the medicines used for anesthesia and sedation in young children. This concern is based on research in animals demonstrating long-term, possibly permanent, injury to the developing brain caused by exposure to these medicines. This injury results in abnormalities in behavior, learning, and memory in animals. The effect of exposure to anesthetic drugs in young children is unknown; however, some but not all studies have suggested that problems similar to those seen in animals could also occur in infants and toddlers. It is important to recognize that the studies in children suggest that similar deficits may occur. These studies in children have limitations that prevent experts from understanding whether the harmful effects were due to the anesthetic drugs or to other factors such as the surgery or related illness. Better research is required to understand whether children are harmed and if so, what alternative medicines might be used to minimize risk from anesthesia.

Because there is not enough information about the effects of anesthetic drugs on the brains of young children, it is not yet possible to know whether use of these medicines poses a risk, and if so, whether the risk is large enough to outweigh the benefit of the planned surgery, procedure, or test. Until further research clarifies the importance of these findings we recommend:

For healthcare providers
Answers to questions from parents and caregivers related to these risks should highlight the differences between research findings in animals and children and the uncertainty of any effect in children. It may also be emphasized that because most anesthetic drugs have been shown to cause injury in animal experiments, no specific medications or technique can be chosen that are safer than any other. Clearly, anesthetic drugs are a necessary part of the care of children needing any surgery, procedure, or test that cannot be delayed. Decisions regarding the timing of a procedure requiring anesthesia should be discussed with all members of the care team as well as the family or caregiver before proceeding. The benefits of an elective procedure should always be weighed against all of the risks associated with anesthesia and surgery.

For parents and caregivers
Discuss the timing of planned procedures with your child's primary care physician, surgeon/proceduralist and anesthesiologist. Concerns regarding the unknown risk of anesthetic exposure to your child's brain development must be weighed against the potential harm associated with cancelling or delaying a needed procedure. Each child's care must be evaluated individually based on age, type and urgency of the procedure and other health factors. Your child's doctors are best able to provide this advice. If you desire additional information and updates on current research, please go to smarttots.org



American Academy of Pediatrics | ASPAN | POSNA | Society for Pediatric Anesthesia | IARS | Pediatric Anesthesia Society | American Society of Anesthesiologists | Pediatric Anesthesia Society of Australia | Pediatric Anesthesia Society of Canada | Pediatric Anesthesia Society of Europe | Pediatric Anesthesia Society of Japan | Pediatric Anesthesia Society of Korea | Pediatric Anesthesia Society of Mexico | Pediatric Anesthesia Society of South America | Pediatric Anesthesia Society of Taiwan | Pediatric Anesthesia Society of Thailand | Pediatric Anesthesia Society of the United Kingdom | Pediatric Anesthesia Society of the United States

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SmartTots was featured in major media outlets during 2015

The New York Times



February 25, 2015

The NEW ENGLAND JOURNAL of MEDICINE

Anesthetic Neurotoxicity — Clinical Implications of Animal Models

Bob A. Rappaport, M.D., Santhanam Suresh, M.D., Sharon Hertz, M.D., Alex S. Evers, M.D., and Beverley A. Orser, M.D., Ph.D.

General anesthetic and sedative drugs are administered to millions of infants, toddlers, and preschool children each year to facilitate life-saving surgery and other essential surgical or medical procedures. In the past two decades, mounting data from animal and observational human

February 26, 2015

JAMA®

Neurotoxicity of Generic Anesthesia Agents in Infants and Children: An Orphan Research Question in Search of a Sponsor

Millions of neonates and toddlers undergo anesthesia or sedation for surgeries and procedures each year. At the same time, mounting evidence from controlled studies in young animals suggests that anesthetic agents administered during vulnerable periods, have neurotoxic effects that result in long-lasting deficits in learning and cognitive behavior. The relevance of these animal models to humans is unclear, and the available observational studies in children are limited. However, the possibility of harm exists. On November 19, 2014, the US Food and Drug Administration (FDA) Science Board, which provides advice to the FDA commissioner, was asked to evaluate whether the emerging data "are sufficient to conclude that the adverse effects noted in juvenile animals are reasonably expected to also occur in developing humans."⁴

April 21, 2015

SCIENTIFIC AMERICAN



June 30, 2015

THE WALL STREET JOURNAL WSJ



December 7, 2015

[Sign up now for your FREE subscription to the SmartTots Newsletter!](#)

Stay abreast of what's being done to make anesthesia safer for infants and children. Each newsletter includes a full compendium of articles representing the latest research in the pediatric anesthesia neurotoxicity field.

SmartTots Newsletter

Archived Articles

[Click here to preview our latest edition](#)

SmartTots successfully launched a vibrant, new website that is an excellent resource for both parents and health care professionals.

SmartTots exhibited at several important conferences throughout 2015:

IARS Annual Meeting and International Science Symposium
Honolulu, HI, March 2015

A highlight for SmartTots at the IARS annual meeting was a presentation by Ansgar Brambrink, MD, PhD entitled *Neurotoxicity of Anesthetics in the Developing Brain – A Translational Update*

Wisconsin Society of Anesthesiologists
WSA Annual Meeting, Milwaukee, WI, September 2015



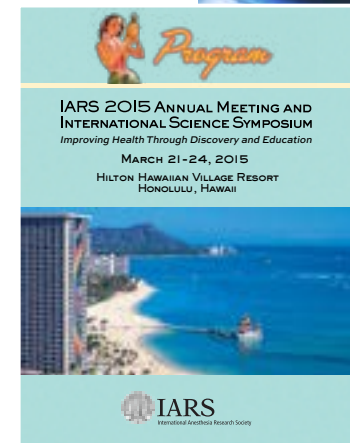
American Society of Anesthesiologists
Anesthesiology 2015, San Diego, CA, October 2015

SmartTots was highlighted at a few key sessions during the ASA annual meeting:

*Dr. Andrew Davidson facilitated a session entitled *Anesthesiology Clinical Trials* where he gave an update on selected high-profile clinical trials, all accepted for publication in *Anesthesiology*. The session also revealed the two year findings of the international, multi-site GAS study.

*In a closed session, Dr. Andrew Davidson provided an update on his T-Rex Pilot study, which is an ongoing study to investigate the use of alternative anesthetics in infants.

*SmartTots funded scientists presented *Neurotoxicity in the Developing Brain: An Update for the Practitioner*.



Look for us in 2016 at the following events:

- April 1 - 3 SPA-AAP Pediatric Anesthesiology, Colorado Springs, CO
- April 16 - 17 PANDA Symposium, New York, NY
- May 21 - 24 IARS Annual Meeting, San Francisco, CA
- SmartTots Panel, Sunday, May 22, 10:30 – 12:00pm
There will be a live stream of this session – learn more at SmartTots.org
- October 21 Society for Pediatric Anesthesia – 30th Annual Meeting, Chicago, IL
- October 20 - 21 Society for Neuroscience in Anesthesiology and Critical Care 44th Annual Meeting, Chicago, IL
- October 22 - 26 American Society of Anesthesiologists – Anesthesiology 2016!, Chicago, IL

And in 2017:

- June 8 - 10 Pediatric Anesthesia and Neurotoxicity
The Second EuroSTAR –
SmartTots Scientific Conference
Genoa, Italy



thank you

Thank you for Investing in Anesthesia Research! SmartTots is extraordinarily grateful for the contributions from our generous donors in support of anesthesia research and would like to acknowledge the donors who contributed in 2015.

\$30,000

American Society of Anesthesiologists

\$2,500 - \$10,000

American Society of Dentist Anesthesiologists

Makoto Ozaki

Michael Roizen, MD and Nancy Roizen, MD

Society for Pediatric Anesthesia

\$500 - \$2,499

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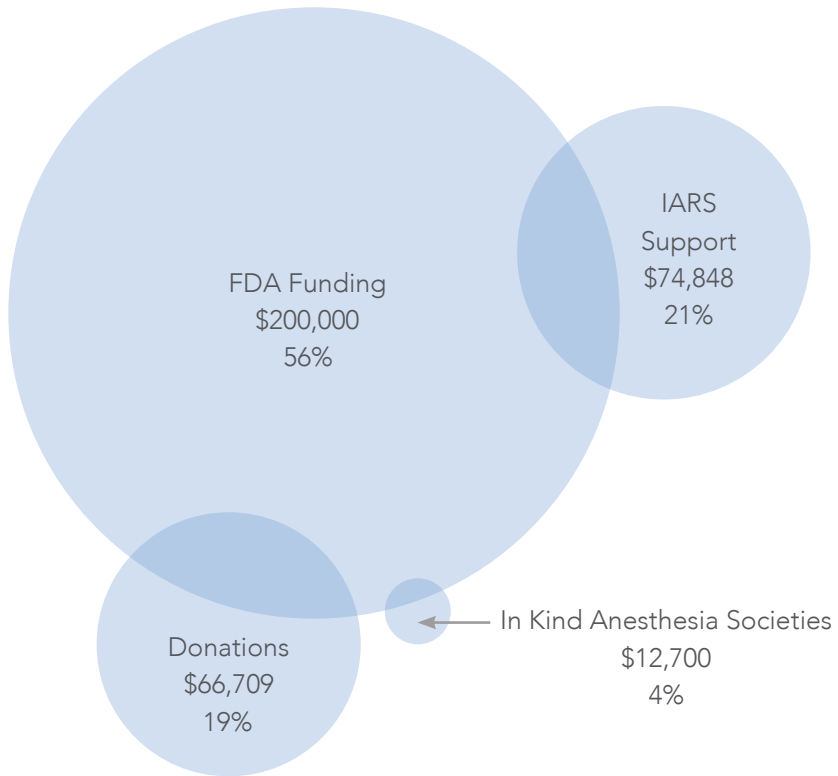
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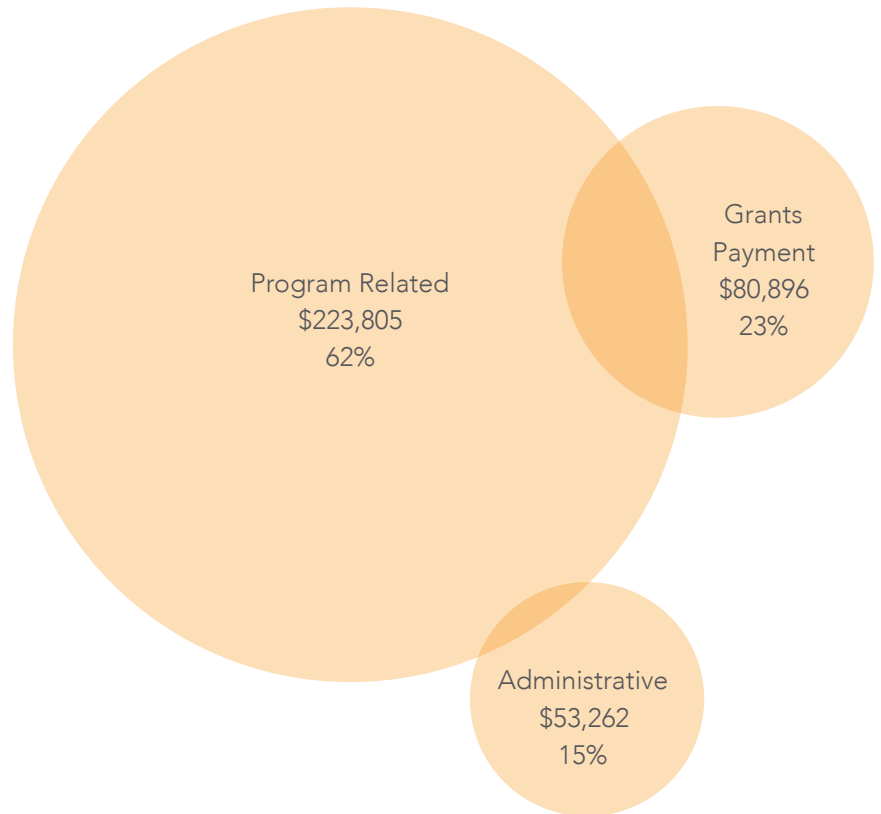
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financial report

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