administration for treatment of spinal muscular atrophy: a single center experience. *Paediatr Anesth*. 2020. https://doi.org/10.1111/pan.13964. Epub ahead of print. PMID: 32623818.
2. Bielsky AR, Fuhr PG, Parsons JA, Yaster M. A retrospective cohort study of children with spinal muscular atrophy type 2 receiving anesthesia for intrathecal administration of nusinersen. *Paediatr Anesth*. 2018;28(12):1105-1108.
3. Greenwald R, Rubin A. Brief assessment of children's post-traumatic symptoms: development and preliminary validation of parent and child scales. *Res Soc Work Pract*. 1999;9:61-75.
4. Nelson JE, Bassett R, Boss RD, et al. Models for structuring a clinical initiative to enhance palliative care in the intensive care unit: a report from the IPAL-ICU project (improving palliative care in the ICU). *Crit Care Med*. 2010;38(9):1765-1772.

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Dexmedetomidine and remifentanil as sole anesthetics in infants: Questionable hypnosis

To the Editor,

We read with concern the article by Efune and colleagues describing the "successful" avoidance of sevoflurane and other agents with putative neurotoxicity in infants by administering dexmedetomidine and opioids instead.[1] This is a worthwhile pursuit; both providers and patient families continue to express concern and confusion about the long-term impacts of anesthetics in infants. However, we contend that the technique described by Efune and colleagues cannot be reasonably compared to potent hypnotic and amnestic agents such as sevoflurane without additional study.

The authors were appropriately concerned about amnesia and hypnosis in the sevoflurane-free group and used processed EEG monitoring, claiming that it indicated likely adequate hypnosis. The evidence for this claim is inadequate. Adult volunteers who received neuromuscular blockade while fully awake had BIS values that incorrectly indicated an anesthetized state.[2] The infants in the study by Efune and colleagues did receive neuromuscular blockade. Moreover, significant limitations exist when using the BIS values to determine the level of consciousness in the developing brain, especially in infants and young children. Although the BIS uses a proprietary algorithm, it is heavily influenced by spectral properties and frequency coherence which are rapidly changing during this developmental period.[3] We advocate against using BIS to provide "reassurance" of the appropriate depth of anesthesia in patients under 2 years of age.

In addition, in adult volunteers it is suggested that the amnesia provided by dexmedetomidine is less effective for stressful memories than for banal memories.[4] Its use as a sole hypnotic and amnestic against the stressors of intubation, muscle relaxation, and surgical stimulus is unproven. We are worried that this may have unknown long-term effects. Despite the lack of explicit memory concerns, stress and pain in infants may result in lasting behavioral change.[5] In fact, the data reported by Efune and colleagues argue that the sevoflurane-free group had inadequate hypnosis. They received an average remifentanil dose of 0.4 mcg/kg/min, without the expected hemodynamic compromise. The use of "light anesthesia" as a surrogate outcome is no panacea. They defined "light anesthesia" as an "increase in heart rate or blood pressure felt to be severe enough by the anesthesiologist to warrant an increase in anesthetic or use of paralytic…" This inadequacy of this surrogate is easily made clear by example. If the children in this study were to receive 1 MAC of inhaled sevoflurane as a sole anesthetic, by definition many or most of them would have skeletal muscle movement and sympathetic activation consistent with "light anesthesia." Despite this, all would have had adequate hypnosis and amnesia, at least based on adult studies on awareness.

In conclusion, a mainstay of anesthesia practice in our era is ensuring analgesia, amnesia, and hypnosis. The data presented in this work are not sufficient to conclude that these children in the two arms of this retrospective study experienced similar levels of amnesia and hypnosis. We suggest that this practice be relegated to careful prospective studies until it is better understood, which at a minimum should compare intraoperative EEG and postoperative behaviors.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

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REFERENCES

1. Efune PN, Longanecker JM, Alex G, et al. Use of dexmedetomidine and opioids as the primary anesthetic in infants and young children: a retrospective cohort study. *Paediatr Anesth*. 2020;30(9):1013-1019.
2. Schuller PJ, Newell S, Strickland PA, et al. Response of bispectral index to neuromuscular block in awake volunteers. *Br J Anesth*. 2015;115(Suppl 1):i95-i103.
3. Akeju O, Pavone KJ, Thum JA, et al. Age-dependency of sevoflurane-induced electroencephalogram dynamics in children. *Br J Anesth*. 2015;115(Suppl 1):i66-i76.
4. Hayama HR, Drumheller KM, Mastromonaco M, et al. Event-related functional magnetic resonance imaging of a low dose of dexmedetomidine that impairs long-term memory. *Anesthesiology*. 2012;117:981-995.
5. Taddio A, Katz J, Ilersich AL, et al. Effect of neonatal circumcision on pain response during subsequent routine vaccination. *Lancet*. 1997;349:599-603.