THE EFFECT OF GENERAL ANESTHETICS AND SEDATIVES ON BRAIN DEVELOPMENT IN CHILDREN

E.S.V. de Sonnaville, MD ¹, M. Königs, PhD², H. Knoester, MD, PhD¹, H. van Ewijk, PhD⁴, K.J. Oostrom, PhD², J.B.M. van Woensel, MD, PhD¹, J. Oosterlaan, PhD^{2,3,4}

¹Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Pediatric Intensive Care, Amsterdam, The Netherlands, ²Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Emma Neuroscience Group, Amsterdam, The Netherlands, ³Emma Children's Hospital, Amsterdam UMC, Vrije Universiteit Amsterdam, The Netherlands, ⁴Vrije Universiteit, Clinical Neuropsychology section, Amsterdam, The Netherlands

Background and aims

- General anesthetics and sedatives are widely used at the Pediatric Intensive Care Unit (PICU).
- Animal studies indicate that exposure of the immature brain to these agents causes neurodegeneration, leading to adverse neurocognitive development. These impairments occur in the most vulnerable brain regions, such as the hippocampus and the anterior thalamus^{1,2}.
- The hippocampus is primarily important in the formation and retrieval of short and long term memory³.
- The anterior thalamus is a key structure for learning, episodic memory and attention⁴
- Effects of general anesthetics and sedatives in children have only been scarcely studied.
- Aim: explore the impact of general anesthetics and sedatives on neurocognitive development in PICU patients.

Methods

Participants

- Exposure group: children aged 6-12 years, admitted to the PICU of the Academic Medical Centre Amsterdam between 2007-2011 with artificial ventilation because of respiratory insufficiency due to lower respiratory tract infections (LRTI). All patients received general anesthetics and sedatives. Viral LRTI almost never manifest neurologically⁵, therefore no neurocognitive sequelae are expected to be caused by the infection itself.
- Control group: healthy peers matched on age, gender and socio-economic status (SES) with exposure group.

Neurocognitive tests

- General neurocognitive functioning: WISC-III full-scale IQ (FSIQ)
- Verbal working memory (WISC-III Digit Span)
- Verbal memory (California Verbal Learning Test)

Table 1. Analyses between Study Groups

n	Exposure	Control	p-value	95% CI		cohen's <i>d</i> (magnitude effect)
	41	41		lower	upper	
<i>Subject characteristics</i>						
Gender			0.12			
Male	24	17				
Female	17	24				
Age at testing, y	8.6 (0.8)	8.9 (1.0)	0.17	-0.84	0.15	
SES	5.6 (1.0)	5.5 (1.0)	0.75	-0.40	0.55	
<i>Neurocognitive outcome</i>						
Estimated FSIQ	96.5 (15.5)	105.3 (16.5)	0.02*	-15.86	-1.78	-0.56 (moderate)
Verbal memory						
Recording capacity	4.4 (1.4)	5.0 (1.5)	0.07	-1.26	0.04	-0.42 (small)
Learning rate	4.6 (2.8)	4.7 (1.9)	0.82	-1.17	0.93	-0.02
Encoding	35.2 (9.3)	39.2 (7.8)	0.04*	-7.79	0.21	-0.47 (small)
Consolidation	13.9 (1.4)	14.0 (1.4)	0.70	-0.76	0.51	-0.07
Retrieval	-7.1 (2.6)	-6.0 (1.8)	0.03*	-2.08	-0.12	-0.50 (moderate)
Verbal working memory and attention						
Total	49.9 (24.6)	56.4 (21.3)	0.21	-16.55	3.67	-0.29 (small)

Values are expressed as mean (SD), * Statistically significant at $p < .05$

Results

As compared to healthy peers, children in the exposure group (Table 1) have:

- Significantly lower FSIQ; and
- Significantly poorer verbal memory, specifically concerning encoding of information in short term memory as well as retrieval of information from long-term memory

Conclusion and future research plans

- Preliminary results suggest that children with a history of PICU-admission and exposure to general anesthetics and sedatives are at risk of decreased global neurocognitive functioning and verbal memory.
- We will further assess the relationship between general sedatives and analgesics on a comprehensive range of neurocognitive functions, behavioral outcome, quality of life and school outcome.

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