

# Are reductions in oxygen to the brain associated with behavioral changes in children undergoing anesthesia?

<b>Submission date</b> 25/08/2021	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 26/08/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 02/10/2023	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Behavioural changes in small children, after general anesthesia, are not uncommon but the causes have not been well elucidated. A previous study from Spain has found an association between such changes and surprisingly small changes in the brain regional oxygen saturation during general anesthesia. If the latter results can be confirmed, it could have major implications on management of children under anesthesia. However, brain oxygen saturation can not always be measured, and reductions are often the result of reduced blood flow and oxygen delivery. Therefore, we aim to investigate the association between brain regional oxygen saturation, and as secondary aim episodes of low blood pressure or peripheral saturation and behavioral changes. We will also check the blood levels of a set of proteins that can be markers of damage to the brain and other tissue.

### Who can participate?

All children between 2 and 6 years of age can participate, if their parents are available to fill in the structured questionnaire (PHBQ) one week after the procedure.

### What does the study involve?

1. Measurement of brain regional oxygen saturation with a NIRS probe - a light sensor that is taped to the forehead when the child is in the operating room.
2. Blood samples are taken when the child is under anesthesia.
3. Recording of behavioral changes according to the PHBQ form, performed by the parents at 1 and 30 days after the procedure

### What are the possible benefits and risks of participating?

There are no direct benefits from participating.

NIRS is non-invasive and without any known side-effects.

The total volume of blood that is taken is around 5 mL which is without risk.

### Where is the study run from?

The pediatric anesthesia section at Uppsala University Hospital, Uppsala, Sweden

When is the study starting and how long is it expected to run for?  
March 2021 to November 2022

Who is funding the study?  
Department of Anaesthesia and Intensive Care and the Gillbergska Foundation, Uppsala, Sweden.

Who is the main contact?  
Associate Professor Peter Frykholm, peter.frykholm@surgsci.uu.se

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr Peter Frykholm

**ORCID ID**  
<https://orcid.org/0000-0001-6402-136X>

**Contact details**  
Dept of Anesthesia and Intensive Care  
Uppsala University Hospital  
Uppsala  
Sweden  
75185  
+46 6171240  
peter.frykholm@surgsci.uu.se

## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**Protocol serial number**  
NIRSKIDS 1.1

## Study information

**Scientific Title**  
Are reductions in cerebral oxygenation associated with postoperative behavioral changes in children undergoing anesthesia?

**Acronym**  
NIRSKIDS

**Study objectives**  
Reduction in crSO<sub>2</sub> of more than 5% from baseline is associated with increased behavioral changes 7 days after general anesthesia

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Approved 15/07/2021, Swedish Ethical Review Authority (Etikprövningsmyndigheten, Box 2110, 750 02, Uppsala, Sweden; +46 10-475 08 00; [registrator@etikprovning.se](mailto:registrator@etikprovning.se)), ref: 2021-02927

## **Study design**

Prospective observational cohort

## **Primary study design**

Observational

## **Study type(s)**

Diagnostic

## **Health condition(s) or problem(s) studied**

Children 2 - 6 years of age undergoing general anesthesia

## **Interventions**

Cerebral oxygenation saturation (crSO<sub>2</sub>) is continuously measured in the operating room starting before anesthesia induction and ending at the end of the procedure when anesthesia has been stopped. The children's parents are asked to fill in a questionnaire on behavioral changes in their child after 1 and 4 weeks postoperatively. The association between crSO<sub>2</sub> changes and behavioral changes are analyzed. Blood samples for analysing markers of cell damage are obtained at the beginning and end of the anesthesia.

## **Intervention Type**

Procedure/Surgery

## **Primary outcome(s)**

1. Behavioral changes according to the Post Hospitalization Behavioral Questionnaire (PHBQ) are measured at 7 days after the general anaesthesia
2. crSO<sub>2</sub> during the general anaesthesia measured using Near Infrared Spectroscopy (Invos, [www.medtronic.com](http://www.medtronic.com)) using an age-appropriate sensor on the forehead

## **Key secondary outcome(s)**

Current secondary outcome measures as of 18/10/2021:

1. Behavioral changes according to the PHBQ measured at 30 days after the general anesthesia. Similarly, the OR of persistent changes is calculated for crSO<sub>2</sub> more or less than 5%.
2. Episodes of hypotension and/or desaturation during anesthesia and PHBQ changes measured using patient records
3. Perioperative behavioural changes: a score of more than 2 of the Pediatric Anesthesia Behavior score at induction and/or a score of more than 14 of the Pediatric Anesthesia Emergence Delirium score in the post-anesthesia care unit.
4. The association between changes in PHBQ and the following biomarkers are investigated at a single time point:
  - 4.1. Neurofilament light chain (NfL) and Glial fibrillary acidic protein (GFAP) measured using

Single molecule array (Simoa) technology (Quanterix, Billerica, MA)

4.2. Ubiquitin C-terminal hydrolase L1 (UCHL1), NGAL, KIM-1, NAG measured using commercial immunofluorescence assay panels

---

Previous secondary outcome measures:

1. Behavioral changes according to the PHBQ measured at 30 days after the general anesthesia. Similarly, the OR of persistent changes is calculated for crSO<sub>2</sub> more or less than 5%.
2. Episodes of hypotension and/or desaturation during anesthesia and PHBQ changes measured using patient records
3. The association between changes in PHBQ and the following biomarkers are investigated at a single time point:
  - 3.1. Neurofilament light chain (NfL) and Glial fibrillary acidic protein (GFAP) measured using Single molecule array (Simoa) technology (Quanterix, Billerica, MA)
  - 3.2. Ubiquitin C-terminal hydrolase L1 (UCHL1), NGAL, KIM-1, NAG measured using commercial immunofluorescence assay panels

**Completion date**

30/11/2022

## Eligibility

**Key inclusion criteria**

Children 2 - 6 years of age scheduled for general anesthesia of at least 30 minutes duration

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Child

**Lower age limit**

2 years

**Upper age limit**

6 years

**Sex**

All

**Total final enrolment**

180

**Key exclusion criteria**

1. Age <2 years
2. Age >6 years
3. Children with significant neurodevelopmental delay
4. General anesthesia <30 minutes
5. Access to the forehead for the NIRS probe unavailable (e.g. neurosurgery)

**Date of first enrolment**

15/09/2021

**Date of final enrolment**

30/06/2022

## Locations

**Countries of recruitment**

Sweden

**Study participating centre****Uppsala University Hospital**

Department of Anaesthesia and intensive care

Uppsala

Sweden

75185

## Sponsor information

**Organisation**

Uppsala Regional Council

## Funder(s)

**Funder type**

Government

**Funder Name**

Region Uppsala

**Alternative Name(s)****Funding Body Type**

Government organisation

**Funding Body Subtype**

Local government

**Location**

Sweden

**Funder Name**

Gillbergiska stiftelsen

**Alternative Name(s)**

Gillbergiska Foundation

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

Sweden

## Results and Publications

**Individual participant data (IPD) sharing plan**

The current data sharing plans for this study are unknown and will be available at a later date

**IPD sharing plan summary**

Data sharing statement to be made available at a later date

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>	Swedish		26/08/2021	No	No