ISRCTN15471325 https://doi.org/10.1186/ISRCTN15471325

Can we detect early changes in brain function and behaviour after anesthesia in infants?

Submission date
23/01/2020

Recruitment status
No longer recruiting

Registration date
03/02/2020

Overall study status
Completed

Last Edited
09/12/2021

Condition category
Surgery

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and aims
Behavioral changes in newborn experimental animals and structural changes in their brains may be caused by most of the common anesthetic agents, shown in numerous experimental studies. There is no clear evidence for such changes occurring also in human babies, but the evidence from animal studies is still a cause for concern. One reason for not finding changes in man may be the lack of methods (up until now) to detect changes early after anesthesia, instead of relying on brain development tests performed several years after the exposure.

The Uppsala Child and Baby Lab have developed methods for detecting changes in brain function in children as young as 6-10 months, and we propose to use these methods to detects subtle changes in brain function. If this works out well, the future aim is to use these methods to develop anesthesia methods with minimal impact on brain function.

In this first study, we aim to investigate if it is possible to detect changes in young children's brain function associated with a single surgical procedure with general anesthesia using the Basic Child project assessments.

Information about the Basic Child project can be found here: https://psyk.uu.se/uppsala-child-and-baby-lab/research/research-projects-basicchild/

Who can participate?
24 otherwise healthy children planned for surgery at 12 months of age are included.

What does the study involve?
At 10 months of age, children will attend the Child and Baby Lab for a baseline evaluation of brain function level. At 12 months, they will have their surgery done as planned, and 6 months later, they are called back to Child and Baby Lab for the same set of brain function tests.

This study is exploratory, and changes in any set of the tests that are part of the Basic Child project may be interesting and open to interpretation in comparison with unexposed children.

In brief, most tests rely on exposing the infant to a stimulus such as a brightly colored object and observing how the infant reacts with eye movement tracking. In some tests, the stimulus is repeated so that the infant´s capability of learning may be tested.

The tests are performed in 30 min sessions with breaks for unorganized play and feeding in between when the parent will be asked to answer questionnaires about their child's level of development and behavior. We will use the Communicative Development Inventories (CDI) to investigate language skills, Vineland II to evaluate functional development. In the weeks after anesthesia, the parents will also be asked to answer the Post Hospitalization Behavior Questionnaire-Ambulatory Surgery.

In all the above tests, we will use measurements of eye movements (www.tobii.com), both with a focus on individual differences as a function of the duration of anesthesia exposure and comparing the exposed cohort's mean scores with a different cohort of unexposed infants.

What are the possible risks and benefits of participating?

No risks are imposed on the infant in this study. No real benefits of participation are expected except increased awareness of the parent about their child's level of development.

Anesthesia exposure is the same regardless of participation in the study.

The tests are performed with the child sitting on the parent's lap. The experience for both infant and parent is very much like play, and our experience is that parents and children seem to enjoy the testing.

Participation could theoretically increase parents' anxiety for the anesthesia due to information about the rationale for the study, but information about effects in experimental animals has been extensively published and the FDA has published a statement about avoiding long anesthetics in young children.

When is the study starting and how long is it expected to run for?
November 2018 to December 2023

Who is funding the study?
Departmental funding from Uppsala University Hospital and the Department of Psychology (Sweden)

Where is the study run from?
The department of Anaesthesia and Intensive Care Uppsala University Hospital (Sweden) and Uppsala Child and Baby Lab, Department of Psychology, Uppsala University (Sweden)

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

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
1

Study information

Scientific Title
Cognitive and behavioral changes after anesthesia in infants. A pilot study.

Study objectives
Subtle changes in cognitive function after general anesthesia at 12 months of age may be detected by a changes in eye movement patterns from pre-exposure to 6 months post-exposure

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/05/2019, Swedish Review Authority (P.O. Box 2110, 75002 Uppsala, Sweden; +46 10 4750800; registrator@etikprovning.se), ref: 21/01/2019

Study design
Longitudinal observational cohort design

Primary study design
Observational

Secondary study design

Longitudinal study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet available in Swedish.

Health condition(s) or problem(s) studied
Infants with a single congenital malformation such as hypospadias or cryptorchidism, scheduled for surgery at 12 months of age

Interventions
Participants will be recruited from infants already recruited to the Basic Child Project. The Basic Child Project assesses 25 cognitive and trait constructs in 120 infants longitudinally from 6 to 30 months of age, with future follow-up in school. The intervention group will include infants with a single congenital malformation such as hypospadias or cryptorchidism, scheduled for surgery at 12 months of age. The control group will include infants who are not scheduled to receive a surgical procedure performed with general anesthesia at the time of recruitment.

Participants in the intervention group are called to Child and Baby Lab, at 10 months of age, for baseline evaluation of brain functional level. At 12 months of age, they will have their surgery done as planned, and 6 months later, they are called back to Child and Baby Lab for the same set of brain function tests.

In brief, most tests rely on exposing the infant to a stimulus such as a brightly colored object and observing how the infant reacts with eye movement tracking. In some tests, the stimulus is repeated so that the infant's capability of learning may be tested.

The tests are performed in 30 min sessions with breaks for unorganized play and feeding when the parent will be asked to answer questionnaires about their child´s level of development and behavior. We will use the Communicative Development Inventories (CDI) to investigate language skills and Vineland II to evaluate functional development. In the weeks after anesthesia, the parents will also be asked to answer the Post Hospitalization Behavior questionnaire.

The control data of subjects without exposure to anesthesia or other exclusion criteria of this study will be obtained from the Basic Child Project database. Children will be studied at 10 and 18 months of age within the Basic Child Project.

This study is exploratory, and changes in any set of the tests that are part of the Basic Child Project may be interesting and open to interpretation in comparison with unexposed children.

Intervention Type
Procedure/Surgery

Primary outcome measure

Any pattern of changes in the tests included in the Basic Child Project measured at 10 months and 18 months of age in the intervention group compared to changes over the same timespan in the unexposed control group.

Baseline measurements take place at 10 months of age, the intervention takes place at 12 months of age and follow-up takes place 6 months later at 18 months of age.

1. Perceptual development is assessed through visual form perception, approximate number system, visual search and pupillary light response at baseline and 6 months
2. Learning capacity is assessed through visual sequencing, associative learning and probability assessment at baseline and 6 months
3. Social behaviour is evaluated through action prediction, action evaluation and gaze following at baseline and 6 months
4. Neurocognitive function and neurodevelopmental level is assessed via eye tracking (cognition: mathematics, physics, probabilities, contingency learning, geometry; social cognition: action prediction, social evaluation, gaze following, biological motion, face perception; attention; motor; pupillary light response, saccade latencies), play scenarios (motor: dynamic reaching, motor development; executive control: inhibition, set-shifting, working memory, pro-sociality /empathy, personality) or during interaction between parents and the child (responsiveness /sensitivity, attachment) at baseline and 6 months

Secondary outcome measures
1. Language skills measured by the Communicative Development Inventories (CDI) questionnaire at baseline and 6 months
2. Functional development measured by the functional evaluation questionnaire Vineland-II at baseline and 6 months
3. Adverse events during anesthesia documented at 6 months
4. Abnormal physiological or care-related events, according to the SAFETOTS 10 N matrix (www.safetots.org) documented at 6 months

Overall study start date
01/11/2018

Completion date
30/06/2023

Eligibility

Key inclusion criteria
1. Single urological congenital malformation such as hypospadias or cryptorchidism
2. Scheduled for surgery at 12 months of age
3. ≤10 months old at time of recruitment
4. Informed consent obtained from parent or legal guardian

Participant type(s)
Patient

Age group
Child

Sex

Male

Target number of participants
24

Key exclusion criteria
1. Syndrome with known neurocognitive function impairment
2. Previous anesthetic exposure
3. Cyanotic heart disease
4. Born before 36 weeks of gestation
5. Cancer
6. A condition that affects the brain such as epilepsy or hydrocephalus
7. Neurosurgical surgery planned
8. Other surgery planned or performed during the study period
9. Parents that do not speak Swedish
10. Parents that have other problems with participation such as functional variation

Date of first enrolment
05/02/2020

Date of final enrolment
30/06/2022

Locations

Countries of recruitment
Sweden

Study participating centre
Uppsala University Hospital
Sjukhusvägen 1
Uppsala
Sweden
75185

Study participating centre
Uppsala Child and Baby Lab, Department of Psychology, Uppsala University
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Sponsor information

Organisation
Uppsala University Hospital

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Sponsor type
Hospital/treatment centre

Website
http://www.akademiska.se/

ROR
https://ror.org/01apvbh93

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Akademiska Sjukhuset

Alternative Name(s)
Uppsala University Hospital

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Results and Publications

Publication and dissemination plan
We intend to publish in a peer-reviewed open-access medical journal after presenting preliminary results at scientific meetings

Intention to publish date
30/06/2024

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date