

# A follow-up of infants born following intrauterine growth restriction: Is there a relation between neonatal cerebral tissue oxygenation and developmental outcome at 4 years?

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|------------------------------|----------------------------|
| <b>Ethical review</b>        | Approved WMO               |
| <b>Status</b>                | Recruitment stopped        |
| <b>Health condition type</b> | Other condition            |
| <b>Study type</b>            | Observational non invasive |

## Summary

### ID

NL-OMON43109

### Source

ToetsingOnline

### Brief title

DINGfu study

### Condition

- Other condition
- Neonatal and perinatal conditions

### Synonym

fetal growth retardation, intrauterine growth restriction (IUGR), ontwikkeling

### Health condition

ontwikkelingsstornissen

## Research involving

Human

## Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Groningen

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** intrauterine growth restriction, near-infrared spectroscopy, neurodevelopmental outcome

## Outcome measures

### Primary outcome

The total IQ based on the Wechsler Preschool and Primary Score of Intelligence (WPPSI) with subdivision into the verbal IQ and the performance IQ.

### Secondary outcome

a) The emotional and social behaviour as assessed with the Children Behavior Checklist (CBCL), the executive functioning assessed with the Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P), and the developmental progress as assessed by the Ages and Stages Questionnaire (ASQ).

b) The DNA methylation using DNA isolated from stool specimens and buccal swabs.

## Study description

### Background summary

Previous studies have suggested that intrauterine growth restriction (IUGR) may expose to neurodevelopmental delay. Furthermore, the degree of cerebral oxygenation monitored with near-infrared-spectroscopy (NIRS) seems to be

related to the range of general movements seen in neonates. This may be related to the degree of fetal brain-sparing resulting from IUGR in pregnancy. There is also some evidence that very high cerebral oxygenation levels (possibly related to extreme brain-sparing) may be related with neurodevelopmental delay just as very low cerebral oxygenation levels. Similarly, DNA methylation of metabolism related loci has been shown to partially depend on oxygen and nutrient supply. On the other hand, the expression of important regulators of oxygen transport (HIF, EPO, EPO receptor) are controlled by DNA methylation. We hypothesize that neurodevelopmental delay at preschool age is associated with both cerebral hypo- and hyperoxia of the newborn with a history of IUGR. We also hypothesize that cerebral oxygenation levels of IUGR infants are significantly associated with changes in DNA methylation.

### **Study objective**

Primarily, to study the relation between neonatal cerebral oxygen saturation and extraction and intelligence at 4 years of age in infants born following intrauterine growth restriction. The second aim is to study the relation between neonatal cerebral oxygen saturation and extraction and behaviour at 4 years of age in infants born following intrauterine growth restriction. Third, the correlation between early oxygen saturation and later differences in DNA methylation will be studied.

### **Study design**

Prospective follow-up study of an IUGR cohort, who previously participated in a study performed in the UMCG with cerebral NIRS measurements (METc nummer 2012-055). Parents will be asked to visit the UMCG with their child for follow-up and to bring a feces specimen of their child for DNA analysis. During the visit the child will be doing an intelligencetest (WPPSI) in the presence of a neuropsychologist or trained medical researcher. We will also perform a physical exam on the child measuring height, weight, head circumference, skin crease thickness, and blood pressure. A buccal swab for DNA analysis will also be taken. While the child will be tested, parents will be asked to fill in three questionnaires (CBCL, ASQ, BRIEF-P) and give information on their socioeconomic status and relevant medical history of the child such as hearing- and visionproblems, psychiatric disorders and neurologic disorders.

### **Study burden and risks**

Data for this study cannot be obtained in another population, as the intention is to study relation between the postnatal cerebral tissue oxygenation and late neurodevelopmental outcome in children born following IUGR. As data on postnatal cerebral tissue oxygenation have already been collected for this IUGR cohort in the context of an earlier study (METC number 2012-055), we will only have to collect data on the neurodevelopment of these children at

preschool/primary school age. Burden and risks associated with the participation in this study are small to non-existent. Participation will require only one visit comprised of an intelligence test (WPPSI) performed in the presence of an experienced paediatric neuropsychologist and three questionnaires which will simultaneously be filled in by the parents/guardian. The tasks and instructions given to the children will be appropriate for their age without overwhelming the child unnecessarily. Children who show resistance will not be forced to participate. The data collected could provide more insight on the predicting value of measured cerebral oxygenation after birth on the neurodevelopmental outcome at preschool/primary school age. DNA methylation, measured in samples obtained in a non-invasive way, could in future potentially serve as biomarkers for tissue oxygenation if correlated. Data also have the potential to make inferences about the actual benefit of brain-sparing often occurring in fetuses with IUGR.

## Contacts

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### Scientific

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Children (2-11 years)

## Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Survivor of the IUGR cohort of a previous study performed in the UMCG, METc number 2012-055
- Near-infrared spectroscopy (NIRS) data available from the first week after birth
- Written informed consent

## Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- Chromosomal disorders
- Congenital infections
- Significantly impaired hearing or vision
- Inability to understand/speak Dutch

## Study design

### Design

**Study type:** Observational non invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Basic science

### Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 13-12-2016

Enrollment: 40

Type: Actual

## Ethics review

Approved WMO

|                    |   |
|--------------------|---|
| Date:              | 10-06-2016  |
| Application type:  | First submission  |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

| Register | ID             |
|----------|----------------|
| CCMO     | NL57199.042.16 |