# Imaging the neurodevelopmental consequences of intrauterine exposure to Antipsychotics and Lithium

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1. To investigate whether children exposed to lithium or antipsychotics in utero have subtle structural brain differences compared to non-exposed children at the age of 8-14 years old (primary objective).2. To investigate whether children exposed to...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Maternal complications of pregnancy |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON47026

**Source**
ToetsingOnline

**Brief title**
The Image_AL study

### Condition

- Maternal complications of pregnancy
- Psychiatric and behavioural symptoms NEC

**Synonym**
Concequences of intrauterine exposure to lithium or antipyschotics

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Antipsychotics, Lithium, MRI, Neurodevelopment

## Outcome measures

### Primary outcome

A Magnetic Resonance Imaging (MRI) brain scan will be performed in children aged 8 years or older at the research location. MR images are required on a 3 Tesla scanner. The scanning protocol will contain a whole-brain structural MRI examination combined with Diffusion Tensor Imaging (DTI) and functional MRI (fMRI). Primary measures will include: intracranial volume, total brain volume, total gray and white matter, volumes of the four cortical lobes and subcortical structures, cerebellar volume, ventricular volume and cortical thickness. Maps of fractional anisotropy will be calculated (DTI).

### Secondary outcome

fMRI:

The fMRI session will include resting state MRI and the Sternberg Item Recognition Task (SIRT) for working memory.

Neuropsychological testing (children from the age of 6 years old):

To examine neuropsychological development of the child we use a selection of subtests from the NEPSY-II-NL assessment.

Cognitive testing:

Intelligence (IQ) of the children and the accompanying parent will be assessed by the Snijders-Oomen Niet-verbale intelligentie Test - Revisie (SON-R 6-40).

Behavioural testing:

For behavioural testing we use the Achenbach System of Empirically Based Assessment (ASEBA) including:

- Child Behaviour Checklist/6-18 (CBCL) is a checklist completed by the parents or a caregiver to identify problem behaviour in the child. The checklist contains 120 questions.
- Youth Self Report (YSR) is a self report checklist completed by the child from the age of 11 years old. The checklist contains questions about skills and emotional and behavioural problems.
- Teacher*s Report Form/ 6-18 (TRF) is a questionnaire filled out by the teacher. It identifies behavioural problems viewed from a teacher*s perspective.

The scores of the CBCL and the TRF will be combined into one total multi-informant score.

- The Social Responsiveness Scale (SRS-2) is a screening instrument designed to assess symptoms of Autism Spectrum Disorders. This questionnaire will be completed by the parent.

Additionally, the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID), a short structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders in children and adolescents, will be administered to all children.

Hormone measurements in hair:

A small string of hair will be obtained from all participants. This will be

used to determine hormone levels (in particular cortisol) in the months prior

to the time of obtainment. Long-term cortisol levels in hair provide a

relatively easy and non-invasive measure of HPA-axis functioning.

# Study description

### Background summary

Patients with bipolar disorder and schizophrenia are usually treated with lithium and/or antipsychotics. Both medications are often continued during pregnancy as discontinuing may induce disease relapse. However, the consequences for the development of the child remain uncertain. Several studies showed minor consequences on pregnancy outcome and congenital malformations. Less is known about the long-term neurodevelopmental consequences of intrauterine exposure to lithium or antipsychotics. The current study will investigate effects of intrauterine exposure to lithium or antipsychotics in children of mothers who used these medications during pregnancy.

### Study objective

1. To investigate whether children exposed to lithium or antipsychotics in utero have subtle structural brain differences compared to non-exposed children at the age of 8-14 years old (primary objective).
2. To investigate whether children exposed to lithium or antipsychotics in utero have functional brain differences compared to non-exposed children at the age of 8-14 years old (secondary objective).
3. To investigate whether children exposed to lithium or antipsychotics in utero have cognitive, emotional or behavioural problems at the age of 6-14 years old (secondary objective).

### Study design

Clinical cohort study examining neurodevelopment after intrauterine exposure to lithium or antipsychotics by MRI and cognitive and behavioural tests.

### Study burden and risks

To our knowledge there are no medical risks associated with an MRI-scan. Since

this study is conducted in children, the actual MRI scan will be preceded by a practice session in a mock scanner. The scanning session should be as pleasant as possible. During the practice session the child will be asked and may indicate (verbal and non-verbal) whether he/she wants to participate in the investigation. The investigation will immediately be ended if the child, the parent or the investigator desires. Both during the practice-session and during the scan, the child is able to watch movies. There are no risks associated with the neuropsychological and cognitive tasks.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

### Inclusion criteria

Children born between 2003-2012:
- Children of mothers treated with antipsychotics or lithium during pregnancy
- Children of mothers diagnosed with one of the following disorders during pregnancy: bipolar disorder, schizophrenia, schizoaffective disorder, psychosis NOS or borderline personality disorder. - Children of mothers who developed postpartum psychosis (PP) after childbirth.
- Children of women who developed schizophrenia within five years postpartum.

### Exclusion criteria

Children will be excluded if they were exposed to both lithium and antipsychotics in utero, or if their mother used recreational drugs or antiepileptic medication during pregnancy.

## Study design

### Design

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|---|---|
| Study type: | Observational invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 12-02-2017 |
| Enrollment: | 441 |
| Type: | Actual |

## Ethics review

Approved WMO

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| Date: | 03-10-2016 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 13-06-2017 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 28-03-2018 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 23-01-2019 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# 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 | NL56845.078.16 |