

# Brain development, brain functioning, growth and metabolic aspects in the clinical management of transsexual adolescents

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<b>Registration date</b> 02/05/2007	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 06/08/2021	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr F.M. Wouters

**Contact details**  
VU Medical Centre  
Department of Pediatrics, 1Y125  
Boelelaan 1117  
Amsterdam  
Netherlands  
1081 HV  
+31 (0)20 444 1035  
f.wouters@vumc.nl

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

N/A

## Study information

### Scientific Title

Brain development, brain functioning, growth and metabolic aspects in the clinical management of transsexual adolescents

### Acronym

Clinical study on transsexual adolescents

### Study objectives

The hypothesis of this study is that the pubertal delay in transsexual adolescents, induced by treatment with Gonadotropin-Releasing Hormone (GnRH) analogues, will cause a difference in the development of brain structures and brain function between transsexuals and age matched control subjects without transsexuality. If cross-sex hormones are added from the age of sixteen, a catch up of brain development is expected. It is of great interest to investigate if this brain development will occur in the direction of the biologic or desired sex.

Gender dysphoria is associated with atypical levels of sex hormones during pregnancy. The hypothesis of this study is that already at a young age, development of brain structures and brain function in gender dysphoric children will occur in the direction of the desired instead of the biologic sex.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Approval received from the local medical ethics committee (Medisch Ethische Toetsingscommissie VU medisch centrum) on the 15th of February 2007 (ref: 2006/292).

### Study design

Observational, parallel group, multicentre, case-control study

### Primary study design

Observational

### Secondary study design

Case-control study

### Study setting(s)

Not specified

### Study type(s)

Not Specified

### Participant information sheet

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

Transsexuality

## **Interventions**

### **Patients:**

Measurements will be performed at a prepubertal stage, before start of GnRH analogue Triptoreline/Decapeptyl-CR (current puberty delaying medication for transsexual adolescents in the VUmc from the age of 12 and if puberty has already started, i.e., Tanner stage B2 in girls, G1-2 in boys), before start of cross-sex hormones (17-beta oestradiol in male-to-female transsexuals and sustanon in female-to-male transsexuals), one year after start of cross-sex hormones and one to two years after gender reassignment surgery.

### **Age matched control subjects (friends of the transsexual patients):**

Measurements will be performed if the transsexual friend starts with puberty delaying treatment, if the transsexual friend starts with cross-sex hormones and one to two years after surgery of the transsexual friend.

### **Interventions:**

1. Structural Magnetic Resonance Imaging (MRI); method used:
  - a. voxel-based morphometry
  - b. Region Of Interest (ROI) analysis
2. Functional MRI (Blood Oxygenation Level-Dependent [BOLD]) during which three cognition tasks will be performed (mental rotation, verbal fluency and emotional faces)
3. Physical examination with anthropometric measurements and gathering of information about pubertal stage according to Tanner
4. Digital photographs and physical appearance list
5. Salivary testosterone measurements
6. Family pedigree research: homosexuality/transsexuality in family

The duration of the intervention will be approximately three hours for any visit, which means at maximum five visits (if patients will be followed longitudinally) for the patients and three visits (if control subjects will be followed longitudinally) for the control subjects.

## **Intervention Type**

Drug

### **Phase**

Not Specified

## **Drug/device/biological/vaccine name(s)**

Triptorelin

## **Primary outcome measure**

1. Cognition: performance and reaction time on three cognition tasks (verbal fluency task, mental rotation task and emotional faces task), reaction times and performance will be measured
2. Functional MRI: data during the verbal fluency task, mental rotation task and emotional faces task
3. Structural MRI: data on total brain volume, grey and white matter (amount and percentage), Cerebrospinal Fluid (CSF), volume frontal and temporal lobe, gyrification, brain asymmetry. ROI analysis of basal ganglia, amygdala, hippocampus, corpus callosum, hypothalamus

The timepoints at which the primary and secondary outcomes are measured for the patients are:

1. Prepubertal stage

2. Before start of GnRH analogue Triptoreline/Decapeptyl-CR (current puberty delaying medication for transsexual adolescents in the VUmc from the age of 12 and if puberty has already started, i.e., Tanner stage B2 in girls, G1-2 in boys)
3. Before start of cross-sex hormones (17-beta oestradiol in male-to-female transsexuals and sustanon in female-to-male transsexuals)
4. One year after start of cross-sex hormones
5. One to two years after gender reassignment surgery

The timepoints for the control subjects are related to the time points of the patients, for they are age-matched friends of the patients. These timepoints are:

1. The moment that the transsexual friend starts with puberty delaying treatment
2. The moment that the transsexual friend starts with cross-sex hormones
3. One to two years after surgery of the transsexual friend

### **Secondary outcome measures**

1. Score from -10 to 10 on handedness questionnaire
2. Performance score on adapted Wechsler Intelligence Scale for Children-III (WISC-III) questionnaire (four items: two performance, two verbal)
3. Information about psychological functioning (parent questionnaire)
4. Anthropometric data, information about pubertal stage according to Tanner
5. Information about homosexuality/transsexuality in family members
6. Digital photographs and physical appearance list (14 items)

The timepoints at which the primary and secondary outcomes are measured for the patients are:

1. Prepubertal stage
2. Before start of GnRH analogue Triptoreline/Decapeptyl-CR (current puberty delaying medication for transsexual adolescents in the VUmc from the age of 12 and if puberty has already started, i.e., Tanner stage B2 in girls, G1-2 in boys)
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1. The moment that the transsexual friend starts with puberty delaying treatment
2. The moment that the transsexual friend starts with cross-sex hormones
3. One to two years after surgery of the transsexual friend

### **Overall study start date**

01/02/2007

### **Completion date**

31/12/2009

## **Eligibility**

### **Key inclusion criteria**

Inclusion criteria - pubertal patients:

1. Girls and boys with transsexualism who are eligible for sex reassignment according to psychologist and psychiatrist (if they are older than 12 years, psychologically stable and live in a

stable social environment)

2. Girls have to be in stage B2 and boys in G2-G3 with measurable oestradiol and testosterone levels respectively

Inclusion criteria - pre-pubertal patients:

1. Girls and boys with high probability of transsexualism according to psychologist or psychiatrist and the age of 9 to 12 years

2. Girls have to be in an earlier stage than B2 and boys in an earlier stage than G2-G3

Inclusion criteria - healthy subjects:

1. Girls and boys who are similar aged friends of the transsexual patients

### **Participant type(s)**

Mixed

### **Age group**

Child

### **Sex**

Both

### **Target number of participants**

264

### **Key exclusion criteria**

Exclusion criteria - patients:

1. Intersex conditions

Exclusion criteria - healthy subjects:

1. Puberty delaying treatment or hormonal therapy; oral contraception users are not excluded

### **Date of first enrolment**

01/02/2007

### **Date of final enrolment**

31/12/2009

## **Locations**

### **Countries of recruitment**

Netherlands

### **Study participating centre**

VU Medical Centre

Amsterdam

Netherlands

1081 HV

# Sponsor information

## Organisation

Vrije University Medical Centre (VUMC) (The Netherlands)

## Sponsor details

Department of Paediatric Endocrinology

P.O. Box 7057

Amsterdam

Netherlands

1007 MB

## Sponsor type

Hospital/treatment centre

## Website

<http://www.vumc.nl/english/>

## ROR

<https://ror.org/00q6h8f30>

# Funder(s)

## Funder type

Industry

## Funder Name

Ferring Pharmaceuticals

## Alternative Name(s)

Ferring

## Funding Body Type

Private sector organisation

## Funding Body Subtype

For-profit companies (industry)

## Location

Switzerland

# Results and Publications

## Publication and dissemination plan

Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Abstract results</a>				No	No
<a href="#">Results article</a>		01/07/2017	06/08/2021	Yes	No
<a href="#">Results article</a>		01/12/2020	06/08/2021	Yes	No
<a href="#">Results article</a>		22/02/2013	06/08/2021	Yes	No
<a href="#">Results article</a>		30/01/2015	06/08/2021	Yes	No
<a href="#">Results article</a>		01/07/2016	06/08/2021	Yes	No