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

Submission date	Recruitment status
02/05/2007	No longer recruiting
Registration date	**Overall study status**
02/05/2007	Completed
Last Edited	**Condition category**
06/08/2021	Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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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
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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 anticonception 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?
Abstract results				No	No
Results article		01/07/2017	06/08/2021	Yes	No
Results article		01/12/2020	06/08/2021	Yes	No
Results article		22/02/2013	06/08/2021	Yes	No
Results article		30/01/2015	06/08/2021	Yes	No
Results article		01/07/2016	06/08/2021	Yes	No