Gender identity, sex hormones & the developing brain

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To compare sex differences in brain functioning using functional magnetic resonance imaging (fMRI) in healthy pre-pubertal boys and girls with a group of children diagnosed with GID. Subjects will have a second fMRI scan, as soon as they enter...

Ethical review	Approved WMO
Status	Completed
Health condition type	Sexual dysfunctions, disturbances and gender identity disorders
Study type	Observational non invasive

Summary

ID

NL-OMON39814

Source
ToetsingOnline

Brief title
Gender identity, sex hormones & the developing brain

Condition

- Sexual dysfunctions, disturbances and gender identity disorders

Synonym
gender dysphoria, gender identity disorder

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: NWO VICI grant

Intervention

Keyword: brain, gender identity, puberty, sex steroids

Outcome measures

Primary outcome

The main study parameter is the Blood oxygen level dependent (BOLD) response in the fMRI tasks.

In the adult participants, the main study parameters are the OAEs and the 2D:4D ratios.

Secondary outcome

Secondary outcome measures are the neuropsychological test parameters, the otoacoustic emission data, self-report data, and hormone level assessments.

Study description

Background summary

The sexual differentiation of the human brain with regard to sexual orientation and gender identity, i.e. the feeling of being a man or a woman, proceeds under the influence of sex hormones during embryonic development. Since the sexual differentiation of the genitals takes place earlier in development than the sexual differentiation of the brain, these two processes may occur independently. It is thus possible that hormone levels are somehow disrupted at the time of brain sexual differentiation which may explain the phenomenon of Gender Identity Disorder (GID), which is characterized by a conviction of having been born in the body of the opposite sex. GID often shows up before puberty. At present, these young GID patients are treated with a GnRH (Gonadotropin-Releasing Hormone) agonist to suppress puberty until they are allowed to start with cross sex-hormone treatment. However, it is unknown whether pubertal hormones influence gender identity. In other words, is gender identity already established during prenatal development or does it need to be consolidated by sex hormones during puberty?
GID often shows up before puberty and is then called *early onset* GID. When the gender dysphoric feelings start after puberty, this diagnosis subtype is called *late onset* GID. Comparison of the two subtypes of GID may provide

information regarding a differential neurobiological aetiology of GID.

Study objective

To compare sex differences in brain functioning using functional magnetic resonance imaging (fMRI) in healthy pre-pubertal boys and girls with a group of children diagnosed with GID. Subjects will have a second fMRI scan, as soon as they enter puberty. In a second experiment, a group of adolescent GID patients will be scanned twice, once before and once during their cross-sex hormone treatment. Sex differences in brain functioning will be compared to a healthy age-matched control group. We will use hypothalamic responses to pheromones as one task since sex differences have been reported in these responses in adults.
By means of a neuropsychological test session and a measure of otoacoustic emissions, gender differences will be assessed on a behavioural as well as physiological level.
The prenatal androgen exposure of a group of adult natal males with GID will be estimated retrospectively by means of measuring OAEs and the second to fourth digit ratio (2D:4D).

Study design

The present study is an observational, longitudinal study, having a within-subjects (repeated measures) 2x2x2 factorial design, with three independent variables: time (1st measurement, 2nd measurement), sex (male, female), and diagnosis of GID (yes, no). Two age groups, peripubertal children and adolescents, will be seen twice during their development.
Two groups of natal men diagnosed with GID, one group with the *early onset* and one with the *late onset* subtype will be compared.

Study burden and risks

Participants are asked to come to the lab two times, for respectively 1,5 hours (screening session) and 3 hours (actual testing session, fMRI experiment). For the screening, subjects are asked to bring early morning saliva and urine samples; they will be seen for a physical examination by a paediatrician, and will receive an olfactory function test.
During the test session subjects undergo a neuropsychological assessment, a measure of click-evoked otoacoustic emissions, and an fMRI session. The risks, associated with participation, can be considered negligible and the burden can be considered minimal. The current study can be regarded as group-related. Because the aim of the study is to investigate the effects of pubertal hormone changes on gender identity and brain function, the participation of pre-pubertal children is required.
Adult participants will be asked for a 15 min test session for the assessment of CEOAEs and 2D:4D measurement. The risks, associated with participation, can

be considered negligible and the burden can be considered minimal.

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
• Patients
- DSM-IV-TR diagnosis Gender Identity Disorder
- 1st measurement: puberty must not yet been reached. Children have to be maximally in Tanner stage 1.
- 2nd measurement: children have to have entered puberty yet. They have to be at least in

Tanner stage 2-3.
- Right-handedness

• Controls
- 1st measurement: puberty must not yet been reached. Children have to be maximally in Tanner stage 1.
- 2nd measurement: children have to have entered puberty yet. They have to be at least in Tanner stage 2-3.
- Right-handedness;Adolescents
• Patients
- DSM-IV-TR diagnosis Gender Identity Disorder
- 1st measurement: patients receive a GnRH-agonist in order to suppress puberty.
- 2nd measurement: patients receive cross-sex hormone treatment
- Right-handedness;• Controls
- Adolescents match in terms of age, sex and educational level with the patient group
- Right-handedness

Adults
• Patients
- DSM-IV-TR diagnosis Gender Identity Disorder
- two measurements: 1) oto-acoustic emissions (OAE), 2) 2D:4D ratios

Exclusion criteria

all subjects:
- Mental retardation (IQ < 70)
- Any kind of hormone therapy intervention
- Anosmia or hyposmia
- Hearing impairment
- MRI contra indications (e.g. a personal of family history of epileptic seizures, past neurosurgical procedures, intracerebral or pacemaker implants, inner ear prothesis or other metal prosthetics/implants, claustrophobia, neurological disorders, severe head trauma, severe behavioural disorders, substance abuse);Patients:
- Co-morbidity, any kind of psychiatric and/or neurological disorders
Controls:
- DSM-IV diagnosis Gender Identity Disorder
- Any kind of psychiatric and/or neurological disorders

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-10-2010
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	20-05-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL31283.029.10