Neural Structure and Function in Tourette Syndrome: distinguishing neural structure and function in Tourette Syndrome from attention-deficit/hyperactivity disorder.

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON41025

Source
ToetsingOnline

Brief title
Neural Structure and Function in TS and ADHD

Condition

- Other condition

Synonym
Tourette's and ADHD

Health condition

ontwikkelingsstoornissen NEG

Research involving
Human

Sponsors and support

Primary sponsor: Donders Institute of Brain, Cognition and Behavior
Source(s) of monetary or material Support: EU FP7 (MARIE CURIE TS-EUROTRAIN)

Intervention

Keyword: Attention-deficit/hyperactivity disorder, Fronto-striatal circuits, Glutamate system, Tourette Syndrome

Outcome measures

Primary outcome

Structural, diffusion and functional (resting state and task specific) MRI

images will be obtained (approx. 60mins). Two neuropsychological tasks will be

performed in an fMRI environment (go/no-go and monetary reward anticipation)

with another 4 tasks completed outside of the MRI environment (motor inhibition

and cognitive flexibility, verbal working memory, motor speed, cognitive

flexibility). Phenotyping will be done by semi-structured interview for the

Yale Global Tic Severity Scale (YGTSS) and Children*s Yale-Brown Obsessive

Compulsive Scale (CY-BOCS). ADHD symptoms will be assessed additionally by

Conners questionnaire.

Secondary outcome

Secundary endpoints are (1) genotypes of candidate genes and (2) lab assesments

of various proteins in blood plasma.

Study description

Background summary

Tourette Syndrome (TS) is a common neuropsychiatric disorder amongst children and adolescents. Attentio-Deficit/Hyperactivity Disorder (ADHD) is often found comorbid with TS, similarly tic disorders often comprise secondary diagnoses in ADHD, making it difficult to eliminate the potential confounds of comorbidity on research findings in TS. Though the frontostriatal circuits and its main regions, the prefrontal cortex and the basal ganglia have been implicated in TS, there are multiple inconsistent findings in studies on structural and functional MRI measures and executive functioning in TS. Glutamate is a major neurotransmitter modulating the activity of the frontostriatal circuits, but its role in TS in unclear.

Study objective

The aim of the study is to acquire MRI, genetic and neuropsychological data on TS subjects. We aim to do this for the purpose of then identifying brain (1) structural, (2) functional and (3) connectivity abnormality differences, and (4) neuropsychological data between subjects with TS, healthy controls, and ADHD to elucidate which neural correlates correspond to each condition, which are common and which unique. Finally (5) glutamate concentrations from the frontostriatal region, acquired with magnetic resonance spectroscopy (MRS), will be compared between healthy controls and ADHD. Secundary exploratory objectives are: identify genetic mechanisms underlying compulsive behaviours in high risk subjects and controls, and identify biomarkers for the compulsivity trait.

Study design

Longitudinal case control study with three groups; (1) TS, (2) ADHD and (3) healthy controls. Participants will be assessed at baseline and again in a similar manner about 3 years after the initial assessment.

Study burden and risks

The burden involves taking part in an MRI scan and having blood drawn once at baseline and once at follow-up three years later. Participants will undergo an hour scanning session in the MRI scanner. The session will be divided into two separate days. There may be some discomfort experienced due to the loud noise of the MRI and being confined to a small space within the bore of the MRI instrument. Furthermore, there may be some discomfort for the patients in recalling psychiatric symptoms and during blood draw. Degree of anxiety and degree of pleasure will be permanently monitored and explicitly asked of parents and children. If children show any resistance the procedure will be stopped immediately.

Risks and physical or physiological discomfort will be negligible and no special risks are associated with this kind of research. Participation in the

study will be of no direct therapeutic benefit to individual patients, however, the study will benefit the population at large, possibly helping future patients with tic disorders. The anticipated scientific merits justify the proposed study.
This research protocol includes the participation of minors. Tic disorders have a childhood onset and often lessen in intensity and frequency or may even disappear during adulthood. The study's goals can only be achieved by studying children as these patterns of behaviour are developing over early adolescence.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

(1) Aged 8 - 12 years at initial inclusion
(2) IQ > 70
(3) Ability to speak and comprehend the native language of the country in which the

assessment takes place
(4) Caucasian descent
(5) Signed informed consent by parents or legal representative
(6) DSM-5 diagnosis of Tourette's Disorder or Persistent (chronic) Motor or Vocal tic Disorder (motor tics only) (APA, 2013).

Exclusion criteria

(1) Intellectual disability (IQ < 70)
(2) Major physical illness of the cardiovascular, endocrine, pulmonal or the gastrointestinal system
(3) All contra indications for MRI assessment, such as the presence of metal objects in or around the body (pacemaker, dental braces)
(4) History of or present neurological disorder

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO

Date:	03-07-2014
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-12-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-04-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL48377.091.14