Compulsive patterns of behaviour in Autism Spectrum Disorder and Obsessive Compulsive Disorder

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Developmental disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON39641

Source
ToetsingOnline

Brief title
Compuls

Condition

- Developmental disorders NEC

Synonym
autism spectrum disorder and obsessive compulsive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: EU FP7 (TACTICS subsidie)

Intervention

Keyword: Compulsive behaviour, Fronto-striatal circuits, Glutamate system

Outcome measures

Primary outcome

Primary endpoints are phenotypic meassures of compulsivity, impulsivity and addiction, and functional and connectivity measures (fMRI, DTI-MR) of striatal and prefrontal regions.

Secondary outcome

Secundary endpoints are (1) genotypes of candidate genes and (2) lab assesments of various proteins in blood plasma.

Study description

Background summary

Compulsivity is a cross-disorder trait underlying phenotypically distinct psychiatric disorders that emerge in (early) childhood (ASD, OCD), or adolescence (addiction to substance use). Compulsivity is defined as the repetitive, irresistible urge to perform a behaviour, the experience of loss of voluntary control over this intense urge, the diminished ability to delay or inhibit thoughts or behaviours, and the tendency to perform repetitive acts in a habitual or stereotyped manner (Chamberlain et al. 2006).
Autism Spectrum Disorders (ASD) are characterized by deficits in (i) reciprocal social interaction and (ii) communication, and by (iii) restricted, repetitive and stereotyped patterns of behaviour, interests and activities. ASD have onset prior to age 3, and a strong persistence over time in childhood, over adolescence and into adulthood.
Obsessive Compulsive Disorders (OCD) are characterized by repetitive thoughts, impulses or images (obsessions) and repetitive behaviours or mental acts (compulsions). It has its onset in late childhood.
Repetitive and compulsive behaviours are core features of both ASD and OCD. In this study the focus will be on compulsive behaviours across the two different clinical phenotypes and the developmental links between compulsivity, impulsivity and addiction.
Compulsivity and the closely associated impulsivity trait are characterized by

behavioural disinhibition maintained by maladaptive fronto-striatal circuits. Increased activity in the striatal components or decreased activity in the prefrontal components may result in an increased automatic tendency for executing impulsive or compulsive behaviours, depending on the sub-component affected. As to date studies have typically investigated prefrontal and striatal areas in isolation, we will focus on abnormalities in functional and anatomical brain connectivity between the various prefrontal components and the components of the striatum.
Furthermore, glutamatergic imbalance in fronto-striatal regions has been observed in childhood OCD. This suggests that impaired functioning of both frontal and striatal areas may be due to a common underlying pathophysiology, such as dysregulation of glutamatergic mechanisms and glutamatergic genes.
The biological determinants that contribute to the pathogenesis of several dysfunctions are poorly defined and no well-characterized biomarkers are available. Therefore, we will also explore potential biomarkers.

Study objective

The two primary objectives are to test the hypothesis that (1) structural and functional abnormalities of the fronto-striatal circuits are related to the development of compulsive and impulsive behaviour in ASD and OCD; and that (2) the glutamate system a key modulator is in these fronto-striatal circuits.
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

This study has a mixed cross-sectional longitudinal design with assessments at two points, three years apart. Measurements will be: MRI (sMRI, fMRI, DTI, rsMRI), MRS, cognition, and behaviour. These measurements will be standardized across four centres (Nijmegen, Utrecht, London, Mannheim). We will study the fronto-striatal circuits by using MRI techniques and study the glutamate system by using MRS.
In addition to extensive MRI and MRS measures, psychiatric and behavioural phenotypes will be collected, including measures of (a) rigid and compulsive patterns of behaviour that are appropriate for these disorders, (b) impulsivity-related behaviours, and measures of (c) addiction. Serum will be collected for genetic analyses and for biomarkers.

Study burden and risks

The proposed study includes an invasive measure, namely the collection of a blood sample, and a MRI session, both at two time points. This is necessary to identify biomarkers for clinical outcome of pharmocological treatment and, at the DNA level, to identify common and rare genetic variants.

Children of 8-12 year will be included in this study, as we are investing the development of compulsive behaviour of early adolescence. This can only be achieved by studying children as these patterns of behaviour are developing over early adolescence.
Participants will undergo an hour scanning session in the MRI scanner. The session will be divided into two separate days. 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. All centres involved have extensive experience with the type of research we are proposing in this protocol and there are no special risks associated with this kind of research. The anticipated scientific merits justify the proposed study. There will be no therapeutic benefit for the participants.

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
(2) For Autism Spectrum Disorder: DSM-IV-TR diagnosis of ASD
(3) For Obsessive Compulsive Disorder: DSM-IV-TR diagnosis of OCD
(4) For Controls: no psychiatric diagnosis and no history of psychiatric illness in first or second-degree familiy members.
(5) Signed informed consent

Exclusion criteria

(1) Mental retardation (IQ<70)
(2) Major physical illness of the cardiovascular, endocrine, pulmonal or gastrointestinal system
(3) All contra indications for MRI assessment (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: Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-04-2014
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	02-08-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-12-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-06-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-09-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-12-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-04-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-05-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-11-2015
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	NL42004.091.12