Facial dysmorphologies associated with CNV expression in psychiatric illness

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Primary objective: To evaluate whether intellectual disability and facial dysmorphology are associated with an increased clinical diagnostic yield of genetic testing among patients with a psychiatric illness.Secondary objective: To investigate the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Neurological disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON48218

Source
ToetsingOnline

Brief title
The FACE Study

Condition

- Neurological disorders congenital
- Mental impairment disorders
- Psychiatric and behavioural symptoms NEC

Synonym
mental retardation, Syndromal psychiatric disorder

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Copy Number Variant (CNV), Facial Dysmorphology, Psychiatric Disorder

Outcome measures

Primary outcome

Quantification of the relationship between psychiatric pathogenic variants and facial dysmorphic features.

Secondary outcome

Multivariate relationship between pathogenic variants (dependent variable), mode of inheritance (independent variable), IQ (independent variable), facial dysmorphic features (independent variable) and psychiatric diagnosis (independent variable).

Study description

Background summary

There is a strong genetic component in the development of psychiatric disorders, but mechanisms of inheritance turn out to be complex. Highly penetrant genetic variations are rare, but recent findings suggest a higher prevalence of pathogenic variants in phenotypically-defined high risk subgroups of patients with psychiatric illness. Pathogenic Copy Number Variants (CNVs) were recently demonstrated to be present in nearly a quarter of patients with syndromic forms of psychiatric disorder (Bouwkamp et al., American Journal of Psychiatry 2017), most prominently involving facial dysmorphology and intellectual disability. Moreover, rare exonic variation has been shown to contribute importantly to psychiatric disease pathogenesis (Genovese et al., Nature Neuroscience 2016; Lek et al. Nature 2016). However, literature on pathogenic CNVs and other rare coding variants in patients with psychiatric illness remains limited, in particular regarding the criteria for implementation of clinical genetic testing. Therefore, the current study will investigate the relationship between psychiatric diagnosis, intellectual disability, dysmorphic facial features and pathogenic genomic variation.

Study objective

Primary objective: To evaluate whether intellectual disability and facial dysmorphology are associated with an increased clinical diagnostic yield of genetic testing among patients with a psychiatric illness.

Secondary objective: To investigate the multi-dimensional relationship between pathogenic genomic variation, intellectual function, facial dysmorphology and psychiatric diagnoses.

Study design

This study will be a naturalistic, multicentre investigation. Clinicians of the participating mental health care centres (Erasmus MC, Antes and *s Heeren Loo) will be informed of the study background and objectives, along with the inclusion and exclusion criteria for enrollment. Additionally, a healthy demographically-matched control group of adults from the general population will be included. Subjects expressing interest to participate in the study will be provided verbal and written information about the study by a member of the research team. After obtaining written informed consent, the study procedure will be performed either at the local clinic at which they were recruited, at the outpatient clinic of the Erasmus MC, or at their home, with the choice of location made by each subject. Blood samples will be drawn for genetic testing and cell banking for future scientific use. Facial morphology will be photographed using the 3dMD Face System and evaluated by a team of experienced clinical geneticists. If a standardized psychiatric diagnosis has not been documented in the medical record, the Diagnostic Interview for Genetic Studies (DIGS) will be performed. If not recently measured clinically (within the prior 5 years), IQ will be assessed by means of the Wechsler Adult Intelligence Scale (WAIS). The maximum estimated time required for the research visit is 3 hours, for which participants will have the option to divide the visit into two visits of 90 minutes each. Parents of the probands, if available, will be asked to cooperate as additional control subjects by providing a blood sample for genetic testing in order to determine whether pathogenic variants identified in the proband are inherited or de novo. Enrollment and examination of all subjects in this study will be conducted over a period of approximately three years.

Study burden and risks

The risks of participation are minimal. Adverse events may include minor bruising or local tenderness at the site of venous blood sampling. No side effects of neuropsychological testing or imaging are known. A recent similar study by this research group suggested there may be potential benefits to the subject. A genetic diagnosis may improve standard-of-care treatment and treatment of medical comorbidity. Subjects and their families often reported a feeling of empowerment after receiving an etiological genetic explanation of the disorder (Bouwkamp et al, 2017) and genetic counselling and testing for

relatives becomes an option. It is important to include patients with intellectual disability in order to study its influence on the rate of copy number variations.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Probands must meet the following criteria:
1. All probands or their representatives must give signed informed consent;
2. Probands have a psychiatric disorder classified according to DSM-IV, DSM-5 or DIGS;
3. Probands are adults, i.e. 18 years of age or older.;Parental controls must meet the following criteria:
1. All parents or their representatives must give signed informed consent.;Healthy controls must meet the following criteria:

1. All healthy controls must give signed informed consent;
2. Healthy controls have no history of psychiatric illness according to DIGS;
3. Healthy controls are adults (i.e. 18 years of age or older), demographically-matched to probands on the basis of age, sex and ethnicity.

Exclusion criteria

1. Unable to give informed consent to all aspects of the study.
2. Unable to speak and be interviewed in Dutch or English (to ensure validity of the interviews).
3. Psychiatric symptoms are secondary to substance abuse;
4. Facial dysmorphology is not congenital.

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:	Pending
Start date (anticipated):	04-03-2019
Enrollment:	240
Type:	Anticipated

Ethics review

Approved WMO

Date:	12-07-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

(Rotterdam)

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	NL68047.078.18