Tackling defective Prefrontal development in Mendelian Syndromes: a compelling (pre-) clinical integrative approach

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First, to define individual as well as group based neurocognitive, psychopathological and behavioural profiles for the RGNS of interest. Second, to develop and evaluate tailor-made interventions that target behavioural problems, psychopathology and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON54120

Source
ToetsingOnline

Brief title
Promise

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Developmental disorders NEC

Synonym
Witteveen-Kolk syndrome; Coffin Siris syndrome; KBG syndrome; FOXP1 syndrome; Brunner syndrome; Wiedemann-Steiner syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: NWA grant to Sharon Kolk (ProMiSe)

Intervention

Keyword: Genetic syndromre, Neurocognitive dysfunction, Neurodevelopmental disorders

Outcome measures

Primary outcome

- Definition of individual neurocognitive, psychopathological and behavioral

profiles associated to specific RGNS.

Secondary outcome

- Definition of group based detailed neurocognitive, psychopathological and

behavioural age-related profiles associated to specific RGNS.

- Create an overview of the applicability of a set of validated, neurocognitive

and behavioural tests adapted to the RGNS.

- Development of tailor-made interventions that target behavioural problems,

psychopathology and quality of life.

- Evaluate the effect of tailor-made interventions on behavioural problems,

psychopathology and quality of life.

- Identify factors that predict effect of intervention.

Study description

Background summary

Rare Genetic Neurodevelopmental Syndromes (RGNS) are frequently accompanied by developmental and behavioural problems and have a negative effect on the quality of life in the patients and their caregivers. Syndrome management

currently mainly focuses on somatic characteristics. However, diagnosis and intervention targeting abnormal behaviour, neurocognitive dysfunctioning and psychopathology may very well improve quality of life and long term outcome. In this study, we will focus on five RGNS, namely Witteveen-Kolk Syndrome (WitKoS), Coffin-Siris Syndrome (CSS), KBG syndrome, FOXP1 syndrome (FOXP1S), Brunner syndrome and Wiedemann*Steiner Syndrome (WSS), because of preliminary evidence for abnormal behaviour, neurocognitive dysfunction and associated psychopathology.

Study objective

First, to define individual as well as group based neurocognitive, psychopathological and behavioural profiles for the RGNS of interest. Second, to develop and evaluate tailor-made interventions that target behavioural problems, psychopathology and quality of life in these RGNS. Third, to create an overview of the applicability of a set of validated, neurocognitive and behavioural tests adapted to RGNS. Fourth, to identify factors that predict effect of the intervention.

Study design

This study is primarily an observational cross-sectional study and uses secondary between-subject design to define group based characteristics as well as a within-subject design to evaluate tailor-made interventions.

Intervention

The tailor-made, non-medical intervention is designed by an experienced multidisciplinary intradisciplinary team, constitutes the regular course of action after diagnoses, also known as standard practice and is targeted at the patient and/or caregivers. It consists of the formulation of treatment goals, psycho-education based on the strength-weakness profile and specific interventions targeting the treatment goals. These interventions are derived from behavioral therapy, cognitive behavioral therapy, acceptance and commitment therapy, Eye Movement Desensitization and Reprocessing and systemic therapy. Treatment will span 7 to 11 sessions of 45 minutes, with a maximum of one session per week and is completed after evaluation at N=1-level.
After completion of personalised patient-focused treatment, a parent-focused treatment will be offered to parents of participants <18 years old with RGNS. The treatment will be offered when parents still report a high lever of behavioural problems after the individualised treatment of the child or when they report high levels of parental stress. This treatment consists of 5 to 11 group sessions of 90 minutes.

Study burden and risks

This study can only be executed in this patient population, by its nature consisting of children and incapacitated adults. All tests and methods used are non-invasive, and all procedures that subjects need to undergo are classified as *procedures with minimal risk and burden* according to the guideline *Toetsing van onderzoek met Minderjarige proefpersonen*.

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)

Inclusion criteria

In order to be eligible to participate in psychiatric and neuropsychological assessment for this
study, all subjects (i.e., participants with RGNS and typically developing

children) must meet
all of the following criteria:
* Biological age above 3 years, because of reliability in diagnostic procedures.
* Written informed consent.
* Ability to speak Dutch.

Additionally a total IQ above 50 is required to be eligible for participation the treatment fase.

In addition to the inclusion criteria stated above, all participants with RGNS must meet the
following criteria:
- Molecular confirmed syndrome diagnosis (i.e. confirmed pathogenic defect in SIN3A,
ARID1B/ARID1A/ARID2/SMARCB1/SMARCA4/SMARCE1/SOX11/SMARCC2, ANKRD11, FOXP1, MAOA or KMT2A)

Exclusion criteria

- Subjects that also have another molecular diagnosis that is likely to contribute to their
developmental phenotype
- Auditory or visual handicap, unable to sit in a chair
- Typical developing participants must not be diagnosed with a mental disorder by the DSM-5 classification system at time of inclusion.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-11-2022

Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	16-11-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-05-2023
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	NL77305.091.21