Executive and social functioning in patients with Tyrosinemia Type 1

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Objective: The main objective of this study is to explore the executive, social-cognitive, and social functioning and behaviour of HT1 patients in relation to present and past tyrosine and phenylalanine levels, history of treatment and treatment...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON47045

Source
ToetsingOnline

Brief title
Executive and social functioning in Tyrosinemia Type 1

Condition

- Metabolic and nutritional disorders congenital
- Inborn errors of metabolism

Synonym
Metabolic disease, Tyrosinemia Type 1

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Swedish Orphan International,Tyrosinemia Foundation (voorheen Stichting Joris) en UMCG

Intervention

Keyword: Executive functions, Research, Social functioning, Tyrosinemia Type 1

Outcome measures

Primary outcome

Main study parameters/endpoints: Neurocognitive tasks, measuring executive functions (inhibition, working memory, cognitive flexibility) and social cognition serve as study parameters. Questionnaires measuring executive and social functioning and behaviour in daily life are also used. Historical and concurrent tyrosine and phenylalanine concentrations are used as predictors expecting significant differences between HT1 patients with high and low blood levels, and between patients and controls.

Secondary outcome

Participants will perform an abbreviated version of the Wechsler Intelligence Scale for Children (WISC) and Wechsler Adult Intelligence Scale (WAIS) with two subtests: Block Design and Vocabulary.

Next to this timing and clinical symptoms at time of diagnosis and some bloodresults will be gathered namely (all other amino acids (including tryptophan), succinylacetone and NTBC concentration, serotonine, prolactin and metanephrines (breakdown of noradrenaline and adrenaline))

Study description

Background summary

Rationale: Patients with Hereditary Tyrosinemia Type 1 (HT1; deficiency of fumarylacetoacetate hydrolase, FAH) usually present with acute liver failure during the first months of life, or (somewhat later) with renal tubular dysfunction with rickets. Originally, HT1 was treated with a tyrosine-phenylalanine restricted diet, usually followed by liver transplantation. Since the discovery of 2-(2-nitro-4-trifluoro-methylbenzoyl)-1,3-cyclohexanedione (NTBC), HT1 patients are treated by NTBC and diet with good outcome with regard to liver disease and renal problems. However, during the past years some preliminary evidence has been provided that these patients are at risk of non optimal neurocognitive outcome. It remains unclear whether these deficits are caused by the disease itself, treatment with NTBC, the resulting high tyrosine, or the low phenylalanine concentrations that are usually seen.

Study objective

Objective: The main objective of this study is to explore the executive, social-cognitive, and social functioning and behaviour of HT1 patients in relation to present and past tyrosine and phenylalanine levels, history of treatment and treatment adherence, and to explore the abovementioned constructs in relation to daily life functioning of HT1 patients (e.g. well-being, quality of life, socio-economic status, friendships and/or relations).

Study design

Study design: Observational cross-sectional between-subjects control group design. A group of HT1 patients will be tested with a wide range of neuropsychological instruments, including executive functioning, social-cognitive, and social functioning and behaviour, taking into account treatment (drug and/or diet).

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Historical tyrosine and phenylalanine concentrations are collected from the databases of the clinical centres and the Dutch patient organization for metabolic diseases in children (Vereniging Kinderen en Stofwisselingsziekte, VKS). Blood samples fall under normal clinical visits and routine control and probably do not have to be taken more often than the HT1 patients are used. Executive functions and social cognition are examined by means of (computerized) tasks which will take a maximum of 2.5 hours. Questionnaires will be filled out to determine executive and social functioning and behaviour in daily life. No physical and physiological discomfort is expected, and no risks are associated with participation in the tasks. The results of the study may help to further determine the

neurocognitive and social profile in HT1 patients.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL

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

General inclusion criteria for recruitment of HT1 patients:
- Patients meet NIH-diagnostic criteria for Hereditary Tyrosinemia Type 1 (HT1)
- Patients are treated with NTBC alone or with a diet as well, or patients received orthotopic liver transplantation (OLT)
- Minimum age of 7 years at time of study
- IQ >= 80 (if unknown, this will be assessed)

- Patients have not participated in neuropsychological studies in the last 6 months
- Native speaker;General inclusion criteria for recruitment of controls:
- Controls are healthy
- Minimum age of 7 years at time of study
- IQ >= 80 (if unknown, this will be assessed)
- Controls have not participated in neuropsychological studies in the last 6 months
- Native speaker

Exclusion criteria

General exclusion criteria for recruitment of HT1 patients:
- Mental retardation that has been diagnosed by the clinical centre
- Neurological damage due to the disease, except for acute porphyria attacks
- Medical illnesses other than HT1 with known effects on cognitive and social functioning
- Not a native speaker;General exclusion criteria for recruitment of controls:
- Mental retardation that has been diagnosed by the clinical centre
- Medical illnesses with known effects on cognitive and social functioning
- Not a native speaker

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:	Health services research

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-08-2012
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO Date:	28-08-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-06-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL41405.042.12