Executive and social functioning in early- and continuously-treated patients with PKU: A follow-up study 10 years later

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

Summary

ID

NL-OMON45119

Source
ToetsingOnline

Brief title
Executive and social functioning in PKU patients

Condition

- Metabolic and nutritional disorders congenital
- Inborn errors of metabolism

Synonym
Metabolic disease, PKU

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Stichting PKU Research;Fonds Nuts Ohra en

UMCG

Intervention

Keyword: Executive functions, Follow-up study, Phenylketonuria, Social functioning

Outcome measures

Primary outcome

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 phenylalanine and tyrosine concentrations, Phe:Tyr ratio, and Phe fluctuation are used as predictors. Significant differences are expected between PKU patients with high and low Phe concentrations, and between PKU patients and controls.

Secondary outcome

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Study description

Background summary

PKU patients are generally on a phenylalanine(Phe)-restricted diet (which prevents mental and neurological retardation) and receive amino acid supplements until early adolescence. After this period, the diet is generally relaxed, resulting in higher Phe levels. As cognitive functioning continues to develop until at least late adolescence/early adulthood, and societal demands (whether social, academic, or work-related) increase during this life phase, it is the question whether relaxation of the diet is harmful or not. Particularly since the mechanisms through which elevated Phe levels affect the brain (i.e., by damaging white matter and by causing dopamine depletion) are in effect throughout life. Moreover, in early- and continuously-treated PKU, an executive function (EF) deficit has consistently been found. It is however the question whether such a deficit extends to other domains of functioning, also for the

younger patients who are still on diet. A question related to both topics mentioned above is whether current treatment guidelines for different age groups should be adjusted in light of the cognitive and social demands in daily life.

Study objective

The main objective of this study is to examine the executive, social-cognitive, and social functioning and behaviour of 7-30 year old PKU patients in relation to history of treatment and treatment adherence. It is expected that there will be significant differences between PKU patients and controls in executive, social-cognitive, and social functioning and behaviour. High Phe concentrations are expected to be related to impairments in these domains. More pronounced differences are expected in the complex executive functions. The second objective is to examine the abovementioned constructs in relation to daily life functioning of PKU-patients (e.g. well-being, quality of life, socio-economic status, friendships and relations).

Study design

Observational longitudinal within- and between-subjects control group design and cross-sectional control group design. PKU patients, who are now young adults, and who underwent neuropsychological assessment approximately 10 years ago are retested, taking into account probable diet relaxation in the last decade, as well as their level of neuropsychological functioning and treatment history at the first assessment. A new group of PKU patients will also be tested with a wider range of instruments (including not only executive functioning, but also social-cognitive and social functioning and behaviour) and more refined indicators of dietary control.

Study burden and risks

Historical phenylalanine concentrations are collected from the data bases of the clinical centres. Blood samples fall under normal clinical visits and routine control and do not have to be taken more often than the PKU patients already have to. Executive functions and social cognition are examined by means of computerized tasks which will take a maximum of 2.5 hours. Questionnaires have to 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 further determine treatment targets in PKU, but the study may also help patients and their environment (partner, work, school) to accept (the consequences of) the disease.

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)
Elderly (65 years and older)

Inclusion criteria

- Patients meet NIH-diagnostic criteria for Hyperphenylalaninemia (HPA) or Phenylketonuria
- PKU patients were treated early (within one month after birth) and continuously (at least until age 12)
- Born after 1974 (start national screening PKU) and minimum age of 7 years at time of study
- Dutch speaking
- PKU patients who use or used Tetrahydrobiopterin (BH4) will not be excluded, but the use of this type of medication (which is being used to treat BH4-responsive HPA/PKU-patients) will be taken into account for statistical analyses (e.g. will be introduced as a covariate in between-group comparisons)

Exclusion criteria

- Mental retardation that has been diagnosed by the clinical centre, or if the IQ is below 80 (after assessment)
- Lack of fluency in Dutch
- Use of medication other than Tetrahydrobiopterin that may affect cognitive functioning
- Medical illnesses other than PKU with known effects on cognitive and social functioning

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:	Recruitment stopped
Start date (anticipated):	23-05-2012
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	08-05-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-12-2012
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Not approved Date:	23-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-12-2017
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	NL38932.042.11