Nutritional deficiencies in children with Attention Deficit/Hyperactivity Disorder: A focus on amino acids

Published: 06-12-2012
Last updated: 26-04-2024

The primary goal of this project is to study whether children with ADHD differ from the normal population on the urinary and plasma levels of the AAA*s (tryptophan, tyrosine and phenylalanine) that are related to the functioning of serotonin and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cognitive and attention disorders and disturbances
Study type	Observational invasive

Summary

ID

NL-OMON39106

Source
ToetsingOnline

Brief title
Nutrients and ADHD.

Condition

- Cognitive and attention disorders and disturbances

Synonym
Attention-deficit/hyperactivity disorder; ADHD

Research involving
Human

Sponsors and support

Primary sponsor: Ansynth Service B.V.
Source(s) of monetary or material Support: Ansynth Service B.V.

Intervention

Keyword: ADHD, Amino acids, Children, Neurotransmitters

Outcome measures

Primary outcome

The primary study parameters are the intake, absorption and excretion of the AAA*s tryptophan, tyrosine, phenylalanine and homocysteine, as measured by a food intake analysis (intake), a plasma analysis (absorption) and a urine analysis (excretion).

Secondary outcome

The secondary study parameters, required to investigate the effects of the levels of the amino acids, are behavioural symptoms of ADHD (ADHD core symptoms and comorbid symptoms), neurocognitive, social-emotional and academic functioning and anthropometric measures.

Study description

Background summary

ADHD is a childhood psychiatric disorder that is characterized by the early onset of age-inappropriate and persistent hyperactivity, impulsiveness and inattentiveness. Despite the field*s scientific progress over the past decades, there is limited insight into the aetiology of ADHD. A dysfunction of the frontostriatal, orbitofronto-striatal, and fronto-cerebellar circuits in the brain has been implicated in ADHD. The serotonergic neurotransmitter system and the dopaminergic neurotransmitter system primarily modulate activity in the frontostriatal, orbitofronto-striatal, and fronto-cerebellar circuits. Recent studies provide evidence for separate contributions of altered functioning of serotonin and dopamine in ADHD. However, the underlying causes of this phenomenon are not clear. The serotonergic system is partly dependent on the availability of the precursor aromatic amino acid (AAA) tryptophan. Studies investigated the tryptophan levels in children with ADHD and suggested that a deficiency of this AAA might play a role in ADHD, yet more research is

required. Therefore, in this study we will investigate the availability of the AAA tryptophan in the body of children with ADHD. Besides, we will investigate the levels of the AAA*s that serve as precursors for dopamine (tyrosine and phenylalanine) and the level of another amino acid (homocysteine) that is related to neurocognitive functioning. Deficiencies in the AAA*s tryptophan, tyrosine and phenylalanine might explain the decreased functioning of serotonin and dopamine in children with ADHD and therefore their deviant behavioural functioning. Meanwhile, large amounts of homocysteine might provide additional predictive value in explaining neurocognitive dysfunctions in ADHD. Investigating the levels of the four amino acids of interest serves three purposes; I) to gain more insight into the aetiology of ADHD, II) to contribute to a more objective assessment of ADHD and III) to provide foundations for investigating alternative treatments for ADHD.

Study objective

The primary goal of this project is to study whether children with ADHD differ from the normal population on the urinary and plasma levels of the AAA*s (tryptophan, tyrosine and phenylalanine) that are related to the functioning of serotonin and dopamine and the amino acid homocysteine. The secondary goal is to study whether the levels of the four amino acids of interest are related to behavioural symptoms of ADHD (ADHD core symptoms and comorbid symptoms), neurocognitive, social-emotional and academic functioning and anthropometric measures.

Study design

In this study the urinary and plasma levels of tryptophan, tyrosine and phenylalanine and the plasma level of homocysteine will be analyzed in a reference group (N=117) and in a clinical group (children with ADHD) (N=94), by means of a 24-hour urine sample and a blood spot. Furthermore, the behavioural symptoms of ADHD, the neurocognitive, social-emotional and academic functioning and anthropometric measures will be investigated in both groups, in order to investigate the associations between the amino acids and the (behavioural) functioning of children.

Intervention

Children are treated with both (1) six weeks of nicotinamide supplementation (an oral dose of 30 mg/kg/day, divided in six equally sized dosages), and (2) six weeks of placebo (an oral dose of 30 mg/kg/day, divided in six equally sized dosages).

Study burden and risks

There are no known risks associated with participation to this study. In order

to analyze the plasma levels of the amino acids we will collect a blood spot in each child. The finger prick to collect a blood spot is considered safe in children and no side effects will be expected. In order to analyze the urinary levels of the AAA*s we will ask children to collect a 24-hour urine sample. Investigating the behavioural symptoms of ADHD (ADHD core symptoms and comorbid symptoms), neurocognitive, social-emotional and academic functioning and anthropometric measures will require time investment of the children (maximum two hours), parents and teachers (maximum fifteen minutes). An important advantage of participation in this study is the possibility for parents to gain insight in possible amino acid abnormalities that may cause increases in behavioural symptoms of ADHD (ADHD core symptoms and comorbid symptoms) and/or deficiencies in neurocognitive, social-emotional and academic functioning and anthropometric measures in their child. Parents will receive a brief report of the results for their child. It will be especially helpful for the families in the clinical group to gain insight into the strengths and weaknesses of their participating child, as ADHD might affect his/her behaviour and performance in several domains. All children will receive a small present. The families in the reference group will receive a sum of fifteen euro for each child that participates, for the insight into the behavioural functioning of the participating child might be of less interest, as few children within the reference group are expected to show deficiencies. This study should be conducted on children rather than adults to be able to study the effect of the amino acid levels on behavioural symptoms of ADHD (ADHD core symptoms and comorbid symptoms), neurocognitive, social-emotional and academic functioning and anthropometric measures, as ADHD is mainly a childhood diagnosed disorder and ADHD has a substantial influence on children, for they are still developing numerous abilities (e.g. social skills and academic abilities). Impairments in the development of these abilities are likely to have an adverse effect on future performance. It is important to get more insight into the underlying causal mechanisms in order to start with early interventions. Furthermore, there is uncertainty about defining features of ADHD in adulthood, which makes it difficult to conduct research within an adult population.

Contacts

Public
Ansynth Service B.V.

Jan Vermeerlaan 202-204
Roosendaal 4703 LE
NL
Scientific
Ansynth Service B.V.

Jan Vermeerlaan 202-204
Roosendaal 4703 LE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

For both groups (the clinical group that consists of children with ADHD and the reference group) the inclusion criteria are that children are (a) between 6 and 13 years old and (b) in grade 1 to 6 from elementary school. Children in the clinical group have received a clinical diagnosis of ADHD, confirmed by standardized assessments.

Exclusion criteria

There is one exclusion criterion for the clinical group and that is that children will not be able to participate when they use methylphenidate (MPH) during the testing. The behaviour and functioning of children should not be influenced by medication when they will be assessed. Children who are receiving a psychopharmacological treatment for ADHD could discontinue their treatment for a short period in order to be able to participate. After the discontinuation of stimulant use, a complete washout will be achieved within 48 hours (Pelham et al., 1999). Therefore, the medication break could be limited to five days (two days before the testing period and three days of testing). Stimulant medication is often discontinued (initiated by parents) during weekends or school-holidays in order to limit the consequences of the negative side effects associated with the use of MPH. The decision for a medication break of five days will be taken in consultation with the responsible psychiatrist of the child.
There will be no exclusion criteria for comorbid disorders that frequently co-occur with ADHD, such as oppositional defiant disorder (ODD), conduct disorder (CD), autism spectrum disorder (ASD) or learning disorders. Using these exclusion criteria would decrease the probability of having a representative sample.

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:	Recruitment stopped
Start date (anticipated):	19-12-2012
Enrollment:	211
Type:	Actual

Ethics review

Approved WMO Date:	06-12-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL39922.029.12

Study results

Date completed: 03-07-2014

Actual enrolment: 187

Summary results
Trial is onging in other countries