Treatment of ADHD with Care as usual versus an Elimination diet: An exploratory investigation on the biological mechanisms underlying the effects of an elimination diet treatment in ADHD

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The main aim of the TRACE-BIOME study is to characterize the role of biomarkers related to the microbiome-gut-brain pathways in the effect of an ED as a treatment for ADHD.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cognitive and attention disorders and disturbances
Study type	Interventional

Summary

ID

NL-OMON42519

Source
ToetsingOnline

Brief title
TRACEBIOME:
an exploratory investigation

Condition

- Cognitive and attention disorders and disturbances

Synonym
ADHD, attention-deficit/hyperactivity disorder

Research involving

Human

Sponsors and support

Primary sponsor: CNS
Source(s) of monetary or material Support: Food & Cognition

Intervention

Keyword: ADHD, elimination diet, microbiome

Outcome measures

Primary outcome

In summary the following measures related to the microbiome-gut-brain axis will

be obtained:

* Microbiome quantity and composition

* Concentrations of shortchained fatty acids

* (Stress) Hormone levels, such as cortisol

* Immunoprofiling, such as concentration of proinflammatory cytokin and

immunoglobulin

* Genotype (DNA/RNA)

Secondary outcome

Controlvariables assessed for TRACE, such as demographics (age, sex)

Study description

Background summary

Previous work has shown that an elimination diet (ED) might be an effective treatment for ADHD. However, the mechanism underlying ED*s effects in ADHD are yet unknown. Converging evidence suggests that the microbiome-gut-brain interaction, involving neural pathways, as well as immune and endocrine mechanisms, plays a crucial role in ED*s effects in ADHD.

Changes in microbiome-gut-brain axis have been suggested to play an important role in neurodevelopmental disorders, such as autism (3). Although direct evidence is currently lacking in ADHD, converging evidence suggests that similar alterations in microbiome-gut-brain interaction can contribute to ADHD symptoms as well. Indeed, not only autism, but also
ADHD has been linked with gastrointestinal abnormalities, which likely reflects alterations in microbiome composition and function. Furthermore, ADHD has been associated with alterations in the endocrine and immune pathways. These alterations in turn have been shown to affect neural development and neural systems implicated in ADHD, such as the dopaminergic system. In a recent study in our research group, we have found a relationship between ADHD, microbiome and brainfunctioning. Since diet plays a crucial role in modulating microbiome composition, there is good reason to believe that ED*s effects in ADHD are mediated by alterations in microbiome-gut-brain interactions.

It is extremely relevant to study the mechanisms underlying ED*s effect in ADHD, and the involvement of the microbiome-gut-brain interaction is the main suspect of these mechanisms. Characterization of the interaction between the intestinal microbiome and the patient is important, as it can ultimately inform clinicians as to potential markers and targets for (preventative) treatment. Furthermore, this knowledge acquisition is an important step in the development of novel nutritional/therapeutic interventions tailored at the individual patient. The previously approved TRACE study (2014-1349) offers an excellent context for taking this step: the food intake will be strictly controlled in the ED condition* patients will be monitored over a long term course of 12-18 months on several outcome measures* the size of the sample is relatively large (n=301).

Study objective

The main aim of the TRACE-BIOME study is to characterize the role of biomarkers related to the microbiome-gut-brain pathways in the effect of an ED as a treatment for ADHD.

Study design

The TRACE study is carried out in three child and adolescent psychiatry centers in the Netherlands: Karakter, Accare and Triversum. Eligible children are treatment naïve children with ADHD 5-12 years old and willing to be randomized to either one of the dietary treatments or the care as usual. The assessments of the TRACE-BIOME study will be synchronized with the three main assessments of the TRACE study, namely at baseline, after 5 weeks of treatment and 1,5 years after start of treatment. Assessments of the TRACE-BIOME study will take place immediately following the main assessments of the TRACE study on the same day, so no extra visit to the clinical center is required.

Intervention

See TRACE (2014-1349):
-Elimination diet
-Control diet
-Care as usual

Study burden and risks

There will be no direct benefits for the participants in this TRACE-BIOME study. By participation, parents and child will help our understanding of the biological mechanisms involved in the ED*s treatment response, which may significantly improve future care for patients with ADHD.

The participants in TRACE-BIOME will be asked to provide extra blood. The venapuncture can be experienced as unpleasant. Note that blood collection by venapunture on each of the main assessment timepoints (T0,T1,T4) has already been approved for the TRACEstudy
in order to determine concentration of nutrients. Thus, there is no additional venapuncture needed for blood collection for the TRACE-BIOME
study* an additional volume of 20 ml (at T0) or 10 ml (at T1 and T4) maximally will be collected in this study. All participants in TRACE-BIOME
will be asked to provide saliva and stool samples. Participants will be allowed to participate in parts of the TRACE-BIOME study instead of the complete protocol. In summary, because the risk is negligible and the burden associated with participation (additional to the approved TRACE study) can be considered negligible, we do not expect (serious) adverse events during this study

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Part of TRACE (20141349):
-clinical ADHD diagnosis according to DSM5 (any subtype)
-ADHD treatment abstinent in past two months
-5-12 years old
-ADHD Rating Scale score higher than 1.5 SD above the mean
-confirmed research diagnosis by a structured psychiatric interview with the parents (KSADS)
-comorbidities are allowed

Exclusion criteria

Part of TRACE (20141349):
-children being treated for ADHD in the past two months (medication, therapy or diet)
-use of any other psychotropic edication
-children and/or parents with inadequate mastery of Dutch language
-eating disorder/diatebes

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-05-2016
Enrollment:	301
Type:	Actual

Ethics review

Approved WMO

Date:	29-12-2015
Application type:	First submission
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	NL55741.091.15