A Two Arm Randomized Clinical Trial comparing the effects of an Elimination Diet and a Healthy Diet in Children with ADHD (TRACE Study). Effects on the Brain * an exploratory investigation

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Objective: The present protocol is nested in the TRACE study (CMO 2014-1349, NL50015.091.14 and in the linked TRACE-BIOME study, CMO 2015-1806, NL53630.091.15), and explores whether an ED, compared to healthy diet, affects the fronto-striatal and...

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

Summary

ID

NL-OMON45989

Source
ToetsingOnline

Brief title
Treatment of ADHD with Care as Usual vs Elimination diet - Brain effects

Condition

- Cognitive and attention disorders and disturbances

Synonym
ADHD, attention-deficit/hyperactivity disorder

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: zonmw,EU Horizon2020 program Grant Eat2beNICE (728018)

Intervention

Keyword: ADHD, fMRI, Randomized controlled trial, Restricted Elimination Diet

Outcome measures

Primary outcome

Main study parameters/endpoints: In TRACE-MRI, the outcome parameters include:

neural architecture (brain structure, function and connectivity (only for

children who are 6 years and older) based on MRI-scans acquired at two

timepoints (T0 en T1) in the Donders Centre for Cognitive Neuroimaging in

Nijmegen.

Secondary outcome

not applicable

Study description

Background summary

Rationale: Food seems to trigger Attention-Deficit Hyperactivity Disorder (ADHD) symptoms in some children and an individually constructed elimination diet (ED) might be an effective treatment for ADHD. It is unknown what the effects of ED are after 12 months and how the effects of ED compare to those of a healthy diet and * in a small comparator arm, care as usual (CAU). This is studied in our ongoing TRACE study (CMO 2014-1349, NL50015.091.14). However, it is still unclear 1) whether food or diet interventions also affect the fronto-striatal and fronto-amygdalar brain systems that are involved in cognitive and emotional control processing deficits whereof are associated with ADHD, and 2) whether effects on these brain systems mediate effects on behaviour.

Study objective

Objective: The present protocol is nested in the TRACE study (CMO 2014-1349, NL50015.091.14 and in the linked TRACE-BIOME study, CMO 2015-1806, NL53630.091.15), and explores whether an ED, compared to healthy diet, affects the fronto-striatal and fronto-amygdalar brain systems, and whether effects on the brain mediate effects on behaviour

Study design

Study design: TRACE uses a patient-preference design where parents/children can choose between diet and care-as-usual (CAU). If they opt for diet they will be randomized to either ED or healthy diet. The proposed TRACE-MRI study will add high quality 3 Tesla MRI assessments (structural MRI, diffusion MRI, functional activations using a stop-signal task and emotional faces (amygdala) task, resting state MRI) at baseline (T0) and endpoint (T1, after 5 weeks of treatment) in the ED and health control diet conditions. The MRI acquisition will as much as possible be combined with the assessments for TRACE, so avoiding extra visits.

Intervention

Intervention of the TRACE study: The ED trajectory consists of a 5-week elimination phase, in which children consume a standardized restricted diet, and a 9-12 months reintroduction phase to find those products triggering ADHD symptoms. Non-responders to ED and children who drop out during the reintroduction phase will be switched to CAU.
Standard intervention to be compared to:
- Healthy diet comparable to a normal dietary pattern prescribed in a strict and structured way, requiring the family, as in ED, to adapt the rules and structure of the family.
- CAU consisting of medication and / or psychosocial interventions.

The TRACE-MRI study will not add any further interventions.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: In the TRACE study, burden for the RED participants are mainly related to the reintroduction phase of the diet, which can take up to 1.5 years, in which ADHD symptoms may re-occur after the reintroduction of a food. Furthermore, all participants and parents are asked to undergo recurrent non-invasive assessments: For children (IQ [once], behavior observation, and cognitive test) the time duration per assessment varies between 1.5 and 2.5 hours (three assessments in total in 1.5 years). For parents (parent-child observation, questionnaires) the time duration of the

begin/end point assessment (T0, T1, T4) is around 60 to 90 minutes and at other time points (T2, T3) around 15 minutes. Finally, all participants will undergo venapuncture (15 ml) at the main assessments to examine potential insufficiencies in nutrients levels, i.e., at at the start of the study (T0), after 5 weeks (T1) and at the end of the study (T4).

The risk of the proposed MRI assessments can be considered as negligible, and the burden for the participants can be considered as acceptable. We have extensive experience in MRI scanning children and adolescents with various psychiatric disorders from age 6 onward, such as in autism (CMO 2013-455, NL45500.091.13), ADHD (CMO 2008-163, NL23894.091.08), and conduct disorders/aggressive behaviour (CCMO 15.0071, NL49997.091.14). We have personnel that has been trained to MRI scan children, is experienced in practising children in the mock scanner, and sensitive to sign of resistance of participants. For TRACE-MRI, the benefits for the participants include good monitoring of treatment effectiveness and the possibility to be treated with an elimination diet free of charge, which is currently not yet covered by health insurance. There will be no direct benefits for the participants in this TRACE-MRI 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. Parents receive ¤30 per assessment for compensation of travel expenses and time investment; children receive a small gift (worth ¤3,-).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-clinical ADHD diagnosis according to DSM-V
-treatment naive
-6-12 years old
-ADHD Rating Scale (ARS) score higher than 1.5 SD above the mean
-conformed diagnosis by structured psychiatric interview (K-SADS) with parents.

Exclusion criteria

- children already being treated for ADHD (either medication or therapy or diet)
- use of any other psychotropic medication
- inadequate mastery of the Dutch language
- presence of claustrophobia
- MRI incompatibility (due to metal parts in the body etc.)

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-01-2019
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	05-11-2018
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	NL65990.091.18