Biomarker Research in ADHD: the Impact of Nutrition: An open-label trial to investigate the mechanisms underlying the effects of a few-foods diet on ADHD symptoms in children

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1) Identify potential mechanism(s) underlying the impact of an FFD on ADHD symptoms;2) Identify biomarkers that predict the response to the FFD.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Psychiatric and behavioural symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON46639

Source
ToetsingOnline

Brief title
BRAIN study

Condition

- Psychiatric and behavioural symptoms NEC

Synonym
HKS (Hyperkinetic Syndrome) hyperactivity

Research involving
Human

Sponsors and support

Primary sponsor: Wageningen Universiteit
Source(s) of monetary or material Support: Subsidie door een goededoelen-stichting die de voorkeur heeft om anoniem te blijven.

Intervention

Keyword: ADHD, Biomarker, Microbiota-Gut-Brain axis, Nutrition

Outcome measures

Primary outcome

ADHD symptoms, measured with validated behavioural questionnaires, in relation to neural activation in the frontal and striatal regions during cognitive tasks measured by functional magnetic resonance imaging (fMRI), abundance of genes encoding phenylalanine and tyrosine metabolism enzymes in the gut microbiota, and peripheral blood levels of phenylalanine and tyrosine.

Secondary outcome

Secondary outcome parameters include the assessment of whole brain neural activation patterns during execution of tasks and functional connectivity at rest, executive functioning, comorbid psychiatric disorders, as well as MGB axis parameters, including taxonomic and functional composition of the gut microbiota, peripheral blood mononuclear cell gene expression, peripheral blood metabolites, peripheral blood protein biomarkers, urine metabolites, and DNA genotype and methylation in buccal cells.

Study description

Background summary

Attention deficit hyperactivity disorder (ADHD) is the most common childhood behavioural disorder, causing significant impediment to a child*s development. The exact aetiology of ADHD, a complex disorder with numerous contributing (epi)genetic and environmental factors, is still unknown. Currently, treatment predominantly consists of behavioural and pharmacological therapy. However, medication use is associated with several side effects and concerns about long-term effects and efficacy exist. Therefore, there is considerable interest in the development of alternative treatment options. Double-blind research investigating the effect of a few-foods diet (FFD) has demonstrated large improvements in ADHD symptoms. However, following an FFD requires great effort of both the child and parents, hence limiting its applicability as an ADHD treatment. To make this treatment easier, more effective or potentially obsolete, we need to understand how and in which children an FFD affects ADHD symptoms. We hypothesise that an FFD affects brain function and behaviour, including ADHD symptoms, and that nutritional impact on brain function is effectuated via the complex network of communication between the microbiota, gut and brain, i.e. the MGB axis.

Study objective

1) Identify potential mechanism(s) underlying the impact of an FFD on ADHD symptoms;
2) Identify biomarkers that predict the response to the FFD.

Study design

An open-label trial with researchers blinded to changes in ADHD symptoms during sample processing and initial data analyses.

Intervention

After a 2-week baseline period (regular diet) participants will follow a 5-week FFD preceded by a 1-week transition period.

Study burden and risks

Previous research has demonstrated that following an FFD can lead to a reduction of ADHD-symptoms. The current study therefore includes a therapeutically active intervention. Participants will follow a 5-week FFD, which may be considered burdensome. During one week in the baseline period and during the FFD phase, parents will record food intake, daily activities and the child*s behaviour; the child will record stool frequency and type. As part of the screening procedure, the paediatrician will verify the ADHD diagnosis or will make a research diagnosis and will conduct a physical examination of the child; children that are deemed eligible for participation will undergo a mock fMRI scan and an intelligence quotient (IQ) test (the latter only if not

conducted in the past year). At the start and end of the FFD, children will undergo: fMRI, Quantitative behaviour test, a buccal swab, blood collection (15 ml), and self-collection of stool and urine samples. Parents will complete questionnaires to monitor ADHD and comorbidities To reduce the burden due to traveling, the child and parents can stay overnight in a hotel in close proximity to the WU, if they wish. This will be directly organised by the WU.
There is a possibility for chance-findings of pathology in the MRI and laboratory analyses or of an indication of a genetic defect during genotyping. Children are not exposed to other risks when participating in this study.
Participants receive the diagnostic FFD research and the IQ-test free of charge; both are currently not or only partially covered by health insurance companies. Travel, hotel and parking expenses will be compensated and children will receive a small gift after each measurement session and an USB drive with an MRI image of their brain after the last fMRI scan.
The personal benefit for participating in the study is the possibility to receive an individually tailored FFD that may reduce ADHD symptoms and often occurring comorbid conditions, which may improve the child*s wellbeing considerably and lead to better future prospects. Moreover, it may diminish (future) medication use and its associated side effects. Most importantly, if this study identifies biomarkers of food-related ADHD or new targets to treat food-related ADHD, the results may potentially lead to novel future diagnostic and/or treatment prospects for children with ADHD, including those participating in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Meeting DSM-IV ADHD criteria
Male
Aged 8 up to and including 10 years
Right-handed

Exclusion criteria

Diagnosis Autism Spectrum Disorder
Diagnosis Developmental Coordination Disorder
Premature birth (< 36 weeks) and/or oxygen deprivation during birth
Diagnosed chronic gastrointestinal disorder, i.e. inflammatory bowel disease, irritable bowel syndrome, celiac disease, non-celiac gluten-intolerance (gluten-sensitivity) or lactose-intolerance
Vegetarian/vegan
Diagnosis dyslexia and/or dyscalculia
IQ < 85
Taking ADHD medication or following behavioural therapy
Use of systemic antibiotics, antifungals, antivirals or antiparasitics in past 6 months
Insufficient command of the Dutch language by either parents or child
Family circumstances that may compromise following or completion of the diet
Having a contra-indication to MRI scanning
Two weeks prior to the start of the study, dietary supplements (e.g. antioxidants, minerals, vitamins) or pro- or prebiotics use have to be stopped.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-02-2018
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	01-02-2018
Application type:	First submission
Review commission:	METC Wageningen Universiteit (Wageningen)

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	NL63851.081.17