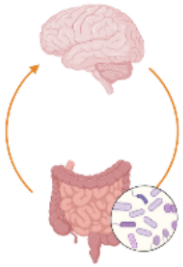
Hôpital Erasme – Hôpital Universitaire de Bruxelles (HUB)
Department of Infant, Child, Adolescent and Young Adult Psychiatry
Clinic for Neurodevelopmental and Learning Disorders



ADHD and the gut-brain axis: exploring the link between gut microbiota, cognition and symptoms

Information sheet and informed consent form for parents

Version 1.1 dated 14/11/2024

English version – translated from the French original

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Principal Investigator	Prof. Dr Isabelle Massat – Child Psychiatrist, Senior Research Associate (FRS-FNRS); Director of the Clinic for Neurodevelopmental and Learning Disorders, HUB
Investigators	Barbara Luyens – Neuropsychologist, PhD candidate Dr François Felgueroso-Bueno – General practitioner, PhD candidate Prof. Dr Véronique Delvenne – Head of the Department of Infant, Child, Adolescent and Young Adult Psychiatry, HUB
Sponsor	Hôpital Erasme – Hôpital Universitaire de Bruxelles (HUB)
Ethics Committee approval	CCB B4062025000026 – Ethics Committee, Hôpital Erasme, Brussels

Study title: ADHD and the gut-brain axis: exploring the link between gut microbiota, cognition and symptoms.

Regulatory sponsor of the study: Hôpital Erasme / HUB

Principal Investigator: Prof. Dr Isabelle Massat

Local investigators: Prof. Dr Isabelle Massat, Dr François Felgueroso-Bueno, Barbara Luyens

Essential information for your decision to participate

Introduction

Your child is invited to take part in a research study led by Prof. Dr Isabelle Massat, Director of the Clinic for Neurodevelopmental and Learning Disorders at the Hôpital Universitaire de Bruxelles (HUB), within the Department of Infant, Child, Adolescent and Young Adult Psychiatry. Her team would like to conduct this study to understand how the gut microbiota, or "gut flora", may be linked to difficulties with concentration and hyperactivity in some children who have ADHD (Attention Deficit Hyperactivity Disorder).

More specifically, this research aims to explore possible differences in the composition of the gut microbiota (or "gut flora") between children with ADHD and typically developing children (without ADHD), as well as the links with their cognitive abilities (concentration, memory, etc.) and their symptoms of hyperactivity, impulsivity and inattention.

To do this, we will analyse a stool sample to study the composition of the gut microbiota. In addition, your child will undergo neuropsychological tests to assess his or her attention (an assessment that is usually recommended when establishing an ADHD diagnosis). Finally, we will ask you to complete a questionnaire to assess symptoms and another questionnaire on your child's eating habits.

Why is this study important? Current research shows that the gut microbiota plays an important role by influencing children's behaviour as well as their attention. Although still few in number, several promising studies have already revealed significant results related to ADHD, highlighting the importance of exploring this line of research further. Understanding this connection could pave the way for new approaches to support children with ADHD, while offering promising therapeutic and preventive perspectives to better understand this disorder.

Who can take part? We invite **children aged 6 to 12 years, with or without ADHD**, to take part in this study.

What participation involves for your child:

- **Clinical work-up**, as is done in usual care (ADHD criteria, various questionnaires, etc.), using clinical criteria such as those found in a standard medical record (age, medical history, etc.).
- **Stool collection**: We will also ask your child for a stool sample in order to analyse the composition of their gut microbiota and compare it between the two groups (ADHD and non-ADHD) to see whether it differs, and to what extent it is associated with their cognitive functioning and with ADHD symptoms/severity.
    - The child will need to do this at home with a small kit that we will provide beforehand, and bring it back to the consultation.
- **Cognitive assessment** administered by a neuropsychologist, entirely standard (tests of concentration, impulsivity, flexibility, etc.), which will be free of charge and covered by the study.
- **Behaviour** or **diet rating scales**, to be completed either by yourself or by the physician.

Summary of the objectives of our study

- ➢ We will compare the **gut microbiota** of children with ADHD with that of typically developing children to see whether it differs: *composition? bacterial signature? imbalance? richness and diversity?*
- ➢ We will explore whether the gut microbiota is linked to certain ADHD symptoms, to their severity and to the children's **cognitive functioning**.

Before you agree to let your child/adolescent take part in this study, we invite you to familiarise yourself with its implications in terms of organisation, benefits and possible risks, so that you can make a fully informed decision. This is called giving "informed consent".

Please read these few pages of information carefully and ask the investigator, or the person representing him or her, any questions you may have.

If you and your child take part in this research, you should know that:

- This clinical study is being carried out following review by the Ethics Committee of the Hôpital Universitaire de Bruxelles (HUB).
- Your participation and that of your child is voluntary and must remain free from any constraint. It requires the signature of a document expressing your consent, as well as your child's. Even after signing it, you may stop taking part by informing the investigator, without having to give any reason. Your decision not to take part, or to stop taking part, in the study will have no impact on your relationship with the investigator. Nevertheless, if you withdraw your consent to the study, the data collected and recorded up to the time of your withdrawal will be kept in order to guarantee the validity of the research. No new data may be collected or transmitted to the sponsor.
- The data collected on this occasion are confidential, and your anonymity and that of your child are guaranteed when the results are published.
- Insurance has been taken out in case you or your child suffer any harm related to your/their participation in this research.
- You can always contact the investigator or a member of her team if you need further information (Tel. Prof. Dr Isabelle Massat 0473807795 / Barbara Luyens 0495744634).

Further information regarding your rights, or those of your child, as a participant in a clinical study is provided in the appendix.

Objectives and conduct of the study

For children/adolescents with ADHD, the assessments will be carried out as usual during medical consultations at the Erasme Medical Center (tel. 02 555 32 96), in the Child and Adolescent Psychiatry outpatient clinic (visits usually required as part of the ADHD diagnostic work-up), and the neuropsychological assessment sessions will be scheduled according to needs (this varies from one child to another).

For typically developing children/adolescents, they will be assessed during the neuropsychological assessment.

At the end of the various tests, you will be able to receive a document (usually an article published in the scientific literature) with the results of this study.

- A stool sample will be collected at home on the day of inclusion or in the days that follow (within the week). This sample will be placed in a small pot containing a stabiliser and handed to the physician or the neuropsychologist at the consultation.

They will store these samples in a −80 °C freezer and, once all the samples have been obtained (recorded in a biobank to meet bioethical requirements), they will be transferred to a laboratory specialised in microbiota analysis, "Walloon Excellence in Life sciences and BIOtechnology, Louvain Drug Research Institute, Metabolism and Nutrition (UCL/LDRI/MNut)", under the responsibility of Prof. Amandine Everard, within the framework of an academic collaboration with UCLouvain.

Description of risks and benefits

All steps comply with good medical practice. There is no risk associated with this study.

The personal benefits include taking part in an innovative study that aims to clarify the links between the gut and the brain in ADHD. This research could pave the way for promising therapeutic and preventive approaches to better treat this disorder.

- You will receive a report on the results of the cognitive assessments. These assessments will be covered by the study. You will not have to pay anything.
- Medical consultations are charged as in usual clinical practice, with INAMI (Belgian health insurance) reimbursement, since the work-up is exactly the same whether or not the child takes part in the study.

If you take part in this research, we ask you:

- To cooperate fully in the smooth running of this research.
- Not to withhold any information about your state of health or your child's, about the medication you or your child are taking, or about symptoms your child is experiencing.
- To inform your physician if you are offered participation in another study, so that you can discuss with him or her whether it is appropriate to take part in that study and whether your participation in the present study should then end.

Contact

If you need further information, or in the event of a problem or concern, you can contact the investigator Dr Isabelle Massat (0473807795, isabelle.massat@hubruxelles.be), Dr Felgueroso-Bueno (tel. 0477929492), or Barbara Luyens, neuropsychologist (tel. 0495744634). The number of the Child and Adolescent Psychiatry outpatient clinic secretariat at the Erasme Medical Center is: 02 555 32 96.

If you have any questions about your rights as a participant in a clinical study, you can contact the patients' rights ombudsman at Hôpital Erasme – 02/555.44.91. If necessary, the ombudsman can put you in touch with the Ethics Committee.

The role of the gut-brain axis in paediatric ADHD: Exploring the links between gut microbiota and cognition.

II. Informed consent

Parent of the participant

I declare that I have been informed about the nature of the study, its purpose, its duration, and what is expected of me and my child. I have read the information document and its appendices.

I have had enough time to think about it and to discuss it with a person of my choice, such as my general practitioner or a family member.

I have had the opportunity to ask all the questions that came to mind and I have received satisfactory answers to my questions.

I understand that my participation and/or that of my child/adolescent in this study is voluntary and that I am free to end my/their participation in this study without this affecting my relationship with the medical team responsible for my child's health.

I understand that data concerning me or my child will be collected as part of my/their participation in this study and that the investigator and the sponsor of the study guarantee the confidentiality of these data.

I consent to the processing of my personal data and/or those of my child in accordance with the terms described in the section on confidentiality guarantees (section III of this document).

I agree / do not agree (**delete as appropriate**) that my general practitioner or other specialist physicians responsible for my child's health may be contacted if necessary to obtain additional information about his or her health.

I agree / do not agree (**delete as appropriate**) that the research data collected for the purposes of the present study may be further processed, provided that such processing is limited to the context of the present study.

I have received a copy of the participant information and informed consent form.

Legal representative of the child

Participant's surname, first name: _____

Father or legal guardian of the participant:	Mother or legal guardian of the participant:
_____	_____
Surname:	Surname:
_____	_____
First name:	First name:
_____	_____
Date and signature:	Date and signature:

III. Appendix "Rights and protection of the participant"

Ethics Committee

This study has been reviewed by an independent Ethics Committee, namely the Erasme-ULB Ethics Committee, which issued a favourable opinion after consulting the Ethics Committee of the Hôpital Universitaire des Enfants Reine Fabiola.

The task of Ethics Committees is to protect people who take part in a clinical trial. They ensure that your rights as a patient and as a participant in a clinical study are respected and that, in light of current knowledge, the study is scientifically relevant and ethical.

Under no circumstances should you regard the favourable opinion of the Ethics Committee as an encouragement to take part in this study.

Voluntary participation

Before signing, do not hesitate to ask any questions you consider useful. Take the time to discuss it with a person you trust if you wish.

Your participation in the study is voluntary and must remain free from any constraint: this means that you have the right not to take part, or to withdraw without justification, even if you had previously agreed to take part. Your decision will in no way affect your relationship with the investigator.

If you agree to take part in this study, you will sign the informed consent form. The investigator will also sign this form, thereby confirming that he or she has provided you with the necessary information about the study. You will receive the copy intended for you.

Confidentiality guarantee

Your participation in the study means that you agree that the investigator collects data concerning you or your child and uses them for research purposes.

In accordance with the Belgian Law of 22 August 2002 on patients' rights, the General Data Protection Regulation (EU 2016/679) of 27 April 2016 (GDPR) and the Belgian Law of 30 July 2018 on the protection of natural persons with regard to the processing of personal data, your child's privacy will be respected and you may, if you wish, have access to the data collected. Any incorrect information can be corrected at your request.

The investigator has a duty of confidentiality with regard to the data collected.

All information collected during this study will be coded (= pseudonymised), so that your child's data can still be linked to his or her personal file. The key to the code assigned to your child will only be accessible to the study investigator (or one of his or her collaborators). Only pseudonymised data will be used in any type of documentation, reports or publications (in the medical scientific literature and/or at medical conferences) concerning this study. Data confidentiality is therefore always guaranteed. Your child's personal data and health data will be processed and stored for a period of at least 25 years.

All data collected during this study are kept in a database managed by the IT Department of the HUDERF.

The database is protected by security measures and a strict access control policy.

The usable personal data are limited to age, gender, level of education, occupation and country of origin.

If you withdraw your consent to take part in the study, the pseudonymised data collected up to the time of your withdrawal will be kept in order to guarantee the validity of the research. No new data may be collected or transmitted to the sponsor.

The Data Protection Officer can provide you with more information on the protection of your personal information. You can contact (please add local contact details):

Representatives of the study sponsor, auditors, the Medical Ethics Committee and the competent authorities, all bound by professional secrecy, may directly access your child's/adolescent's medical record under the responsibility of the investigator (or one of his or her collaborators) in order to check the study procedures and/or the data collected, without breaching confidentiality. This is only possible within the limits of the relevant laws. By signing the consent form, and after having received the prior explanations, you also consent to this access.

You have the right to lodge a complaint about how your information is handled with the data protection authority:

Data Protection Authority (Autorité de protection des données, APD)
Rue de la Presse 35,
1000 Brussels
Tel. +32 2 274 48 00
e-mail: contact(at)apd-gba.be
Website: www.autoriteprotectiondonnees.be

If you decide to take part in this study, we will inform your general practitioner only to the extent that you wish.

If you discontinue the study, the coded data collected up to the time of your discontinuation will be kept in order to guarantee the validity of the research.

Insurance

In this interventional study, the possible risks could include a breach of the measures taken to protect the confidentiality of private information concerning you, as well as psychological discomfort following the completion of the various questionnaires and tests. The sponsor assumes, even without fault, liability for any harm caused to the participant (or his or her beneficiaries) and directly or indirectly linked to participation in this study. To this end, the sponsor has taken out an insurance contract.