Dietary supplement, gut microbiota and ADHD

Study sponsor: Hôpital Erasme / HUB

Principal investigator: Prof. Dr Isabelle Massat

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

The research team of Prof. Dr Isabelle Massat, Director of the Neurodevelopmental and Learning Disorders Clinic at the Hôpital Universitaire de Bruxelles (HUB), within the Department of Infant, Child, Adolescent and Young Adult Psychiatry

Information and Informed Consent Form for Parents

Participant with ADHD

Version 1.1 – 22/08/2025

Research project number: HUB2025312

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Study title: Dietary supplement, gut microbiota and ADHD (short title: Gut microbiota and ADHD)

Target population of this form: Parents / legal representatives of children aged 6 to 12 years with ADHD

Study site: Erasme Medical Center – Child and Adolescent Psychiatry Outpatient Clinic, Hôpital Universitaire de Bruxelles (HUB)

Contents: I. Introduction — II. Informed consent — III. Annex "Rights and protection of the participant"

English translation of the French document "Formulaire d'information et consentement éclairé pour les parents – version 1.1" dated 22/08/2025 (HUB2025312_ICF_FR_PARENT_TDAH). Original language: French. In the event of discrepancy, the French version approved by the Ethics Committee prevails.

I. Introduction

Your child is invited to take part in a research study led by Prof. Dr Isabelle Massat, Director of the Neurodevelopmental and Learning Disorders Clinic at the Hôpital Universitaire de Bruxelles (HUB), within the Department of Infant, Child, Adolescent and Young Adult Psychiatry.

Her team wishes to conduct this study in order to understand how the gut microbiota, or "intestinal flora", may be linked to the difficulties with concentration and hyperactivity experienced by some children with ADHD (Attention-Deficit/Hyperactivity Disorder). In addition, there is a dietary supplement (Pycnogenol), an extract of maritime pine bark, which could help to improve hyperactivity and/or impulsivity and/or concentration, as a complement to the other management measures proposed. https://www.pycnogenol.com/home/

We will therefore explore whether taking Pycnogenol helps to improve symptoms while modifying the intestinal flora, in order to understand the mechanisms of action of this dietary supplement.

This research aims specifically to explore possible differences in the composition of the gut microbiota (or "intestinal 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.

Neuropsychological tests will be carried out in order to assess your child's attention (an assessment that is usually recommended during the diagnostic work-up for ADHD). This assessment will be carried out twice, 10 weeks apart, in order to see whether improvements can be observed. We will also ask you to complete questionnaires to assess your child's symptoms and dietary habits, as well as the consistency of his or her stools. We will give you a box of Pycnogenol, and your child will have to take one tablet in the evening at mealtime.

We will analyse a stool sample on several occasions (at the time of the first neuropsychological assessment, then at week 5, then at the end of the study at week 10) in order to study the composition of the gut microbiota.

Why is this study important? Current research shows that the gut microbiota plays an important role by influencing children's behaviour and attention. Although still few in number, several promising studies have already revealed significant findings in relation to ADHD, underlining the importance of pursuing this line of research. Understanding this connection could pave the way for new approaches to supporting children with ADHD, while offering promising therapeutic and preventive perspectives for a better understanding of 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:

- A clinical work-up, as performed in routine care (ADHD criteria, various questionnaires, etc.), using clinical criteria such as those contained 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 the 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 cognitive functioning and with the symptoms/severity of ADHD. Your child will need to do this at home with a small kit that we will provide beforehand, and bring it back to the consultation.
- A cognitive assessment administered by a neuropsychologist, entirely standard, which will be free of charge and covered by the study. This assessment uses computerised tests to evaluate concentration in various ways (how long the child can concentrate, the ability to concentrate on 2 tasks at the same time, spatial attention, organisation, planning, working memory, mental flexibility (the ability to switch from one instruction to another)).
- Behavioural, dietary or stool-consistency 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.
- ➢ We will explore the effect of the dietary supplement Pycnogenol as an aid to improving ADHD symptoms, and see whether this improvement is associated with a change in the intestinal flora (which we analyse in the stools).

Before you agree to your child/adolescent taking 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 implemented after review by the Ethics Committee of the Hôpital Universitaire de Bruxelles (HUB).
- ➢ Your participation and that of your child are voluntary and must remain free of any constraint. It requires the signature of a document expressing your consent, as well as your child's. Even after signing, you may stop taking part by informing the investigator, without having to justify your decision. 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 retained 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 should suffer harm related to your/his or her participation in this research.
- ➢ You may contact the investigator or a member of her team at any time if you need further information (Tel. Prof. Dr Isabelle Massat / Barbara Luyens on 02553296).
- ➢ You will not receive the results of the analysis of your child's gut microbiota as, to our knowledge, these have no clinical value at the individual level.

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

Objectives and conduct of the study

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

Once the various tests have been completed, you will be able to receive a document (usually an article published in the scientific literature) presenting the results of this study.

- ➢ A stool sample will be collected at home (with kits that we will give you) on the day or days following inclusion (within the week), then at week 5, then at week 10 (at the end of the study). This sample will be placed in a small container containing a stabiliser and handed over at the consultation to the physician or the neuropsychologist.

They will store these samples in a −80 °C freezer and, once all the samples have been obtained (recorded in a biobank in order 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. The stool sample will be destroyed after analysis of the gut microbiota, which makes its use in any other study impossible. Should additional analyses be required, they would be submitted to the Ethics Committee for approval.

Description of risks and benefits

All steps comply with good medical practice. There is no particular risk associated with this study, except possibly some abdominal cramps (as when eating too much fruit) related to taking Pycnogenol. This is very infrequent, and Pycnogenol can be stopped immediately, even without the physician's agreement (but the physician must be informed, and the child then leaves the study).

The personal benefits include taking part in an innovative study that aims to clarify the links between the gut and the brain, under the influence of Pycnogenol, a natural dietary supplement, 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 have nothing to pay.
- Pycnogenol will be provided to you for the duration of the study, free of charge, i.e. for 10 weeks.
- Medical consultations are billed as in routine clinical practice, with INAMI (Belgian national 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 proper conduct of this research.
- Not to withhold any information about your own health or that of your child, about the medications that you or your child are taking, or about any symptoms your child is experiencing.
- To inform your physician if you are invited to take part in another study, in order to 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, but also in the event of a problem or concern, you may contact the investigator, Prof. Dr Isabelle Massat, via the secretariat of the Child and Adolescent Psychiatry Outpatient Clinic at Erasme Medical Center on 02 555 32 96 and by e-mail at isabelle.massat@hubruxelles.be.

If you have questions regarding your rights as a participant in a clinical study, you may contact the patient rights ombudsman at Hôpital Erasme – 02/555.44.91. If necessary, the ombudsman can put you in contact with the HUB Ethics Committee.

II. Informed consent

Parent of the participant with ADHD

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

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

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/his or her 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/his or her 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 further 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 processed at a later date, 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

Surname, first name of the participant: _____

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. Annex "Rights and protection of the participant"

Ethics Committee

This study has been reviewed by an independent Ethics Committee, namely the Ethics Committee of the HUB.

The task of the Ethics Committee is to protect the people who take part in a clinical trial. It ensures that your rights as a patient and as a participant in a clinical study are respected and that, in the 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 inducement 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 of 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 to the investigator collecting data concerning you or your child and using 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, or GDPR) of 27 April 2016 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 may 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 record. The key to the code assigned to your child will be accessible only to the study investigator (or one of his or her collaborators). Only pseudonymised data will be used in any documentation, reports or publications (in the medical scientific literature and/or at medical conferences) concerning this study. The confidentiality of the data 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 by 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 retained 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 may contact (please add local contact details): dpo@hubruxelles.be

Representatives of the study sponsor, auditors, the Medical Ethics Committee and the competent authorities, all bound by professional secrecy, may have direct access to 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 possible only 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 processed with the data protection authority:

Data Protection Authority (APD/GBA)
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 retained 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 in the absence of fault, liability for harm caused to the participant (or his or her beneficiaries) and directly or indirectly related to participation in this study. To this end, the sponsor has taken out an insurance policy.