Participant information for participation in a scientific study

Brain and glycemic responses to sweet soft drinks (SweetBrain)

Official title: Brain and glycemic responses to soft drinks with different sweeteners.

Introduction

Dear Sir/Madam,

With this information letter we would like to ask you if you would like to participate in a scientific study. Participation is voluntary. You can read about the details of the study, what it means for you, and what the advantages and disadvantages are. It is a lot of information. Would you like to read through the information and decide if you want to participate? If you want to participate, please fill out the form found in Appendix C.

Ask your questions

You can make your decision with the information found in this information letter. In addition, we encourage you to:

- Ask questions to the researcher giving you this information.
- Talk to your partner, family or friends about this study.
- Ask questions to the independent expert, Dr. Jeroen Nikken.
- Read the information at https://english.ccmo.nl/human-subjects.

1. General information

This research is being conducted by the Division of Human Nutrition and Health of Wageningen University in collaboration with Tate&Lyle. Tate&Lyle is paying for this research. It requires 30 study participants and takes place on the Wageningen University campus and in the Gelderse Vallei Hospital (Ziekenhuis Gelderse Vallei (ZGV). The Medical Ethics Review Committee METC Oost-Nederland has approved this research.

2. What is the purpose of the study?

The purpose of this study is to better understand the effects of drinks with different sweeteners on brain activity and bodily processes (gastric emptying and blood sugar and insulin levels).

3. What is the background of the study?

There is an increasing trend of replacing sugars with low-calorie sweeteners in soft drinks. This is mainly done to reduce energy intake from drinks. This can help to reduce energy intake and prevent weight gain. There are many different low-calorie sweeteners. We know that they are processed differently in the body, but there is still a lot that we do not know. This study examines for several drinks with low-caloric sweeteners how they affect brain activity, gastric emptying and blood sugar and insulin levels. We want to know in how far these responses resemble those to water and an equally sweet sugar drink.

4. What participation involves

How long will the study take?
Are you participating in the study? Then it will take about 8 weeks in total.

Step 1: Are you eligible to participate?
First we want to know if you are eligible to participate. That is why the researcher tests. To participate, you must meet all of these **inclusion criteria**:

- Being 18 - 30 years old
- Having a BMI between 18.5 - 25 kg/m^2
- Being healthy (self-reported)
- Being right-handed (because brains of left-handed people might differ from brains of right-handed people)
- Sufficient blood hemoglobin (Hb) levels (women > 7,5; men > 8.5 g/dl) and having veins suitable for blood sampling via a catheter. Hb will be measured in a blood droplet obtained with a fingerprick during the screening session.
- Agreeing to be informed about chance findings that might suggest you have a disease and agreeing to let your general physician know about this

You cannot participate if you meet any of the following **exclusion criteria**:

- Having disturbances of glucose metabolism such as being prediabetic or diabetic
- Having an allergy or intolerance for sucrose, sucralose, stevia, allulose, or monk fruit
- Currently following or having followed calorie-restricted diet in the past two months
- Being a regular smoker (more than one cigarette or e-cigarette with nicotine per day)
- Drinking more than 14 glasses of alcohol a week

- Having genetic, psychiatric or neurological disease affecting the brain
- Having gastric disorders or regular (more than once a week) gastric complaints, for example heart burn
- Having renal or hepatic disease
- Using recreational drugs more than once per month
- Having given a blood donation in the past two months
- Being pregnant, lactating or planning on becoming pregnant during the study
- Being a student or employee of the Division of Human Nutrition and Health of Wageningen University
- Participating in another medical-scientific study during the study period

Further exclusion criteria, related to the MRI scanning are:

- Having a fear of tight spaces (claustrophobia)
- Having a contra-indication to MRI scanning (including, but not limited to):
    - Pacemakers and defibrillators
    - Metal objects on/in the head that cannot be removed
    - Implants that respond to magnets

What happens during the screening?

The screening takes place in the Helix Building, located on the Wageningen University campus and lasts approximately 30 minutes. During the screening session, you will first sign a consent form (Appendix C). We will then determine if you are eligible to participate. You will receive a questionnaire in which we ask you if you are in good health, are taking any medications that may affect the results and if you are hypersensitive to any of the ingredients. You cannot participate if you smoke regularly. We also check if there are reasons why you should not be in an MRI scanner (for example, metal in the body or a pacemaker). We also measure the iron (Hb) level in your blood. We measure this with a finger prick (one drop of blood). We do this to make sure your iron level is high enough to take blood samples in the study. Finally, you will lie down in a non-working model of an MRI scanner (dummy scanner) and experience drinking in this position by drinking 250 ml of water through a tube.
If the questionnaire and blood test show that you can participate, and you still want to participate, you will be asked to fill out some questionnaires about your usual eating and drinking habits. Finally, we will make the first appointments for the MRI scan sessions. We ask you to have the same type of evening meal the night before each session.

Step 2: the intervention

The study consists of 6 test sessions on different days. On each test day, you will drink 500 ml of a sweet soft drink (no soda) or water. You will be given a different drink at each visit.

Step 3: measurements

The study consists of 6 test sessions of about 100 minutes spread over different days, a total of 10 hours. You will find more information about the sessions below.

During each session, we measure your brain activity and stomach contents using MRI (Magnetic Resonance Imaging). MRI is a widely used medical imaging technique that can show the anatomy and functions of the body and brain. We do this before and after consuming 500 ml of a sweet drink or water. We also take 6 blood samples at 5 of the testing sessions to measure your blood sugar and insulin levels.

What is MRI and what does it involve?

Magnetic Resonance Imaging (MRI) is a medical imaging technique used for imaging the body and certain body processes. An MRI scanner uses a strong magnetic field and radio waves to produce images. It is a safe, painless procedure that is commonly used to diagnose diseases without the use of radiation such as X-rays or ionizing radiation. Having an MRI scan involves hearing loud noises (this is reduced by wearing ear protection), mild restraint to limit head movement (your head is inside an MRI coil which somewhat resembled wearing a motorbike helmet), and being in a strong magnetic field, which you will not feel. In this study we make different brain scans: an anatomical scan that shows what your brain looks like; a scan that shows what your stomach looks like; a scan that measures the blood flow in your brain and a scan that measures which parts of the brain communicate more with each other.

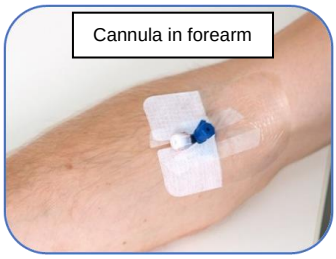
What happens during the scanning sessions?

The scanning will take place in our MRI facility at the Radiology Department of Hospital Gelderse Vallei (Gelderse Vallei Hospital), in Ede.

1. On the morning of the test sessions you will come to the hospital sober, which means that the evening before after 10:00 p.m. you are not allowed to eat or drink anything except water. In the last 90 minutes before the session, you may not consume anything; it is very important that you arrive with an empty stomach.

   First, you will complete an MRI safety form to make sure you do not have any metals in or on your body (such as piercings). If you are wearing clothing that is not suitable for in the MRI (i.e., clothing with metal parts that cannot be removed), you will be asked to change into MRI-appropriate clothing provided to you by us.

2. Blood collection: a cannula will be inserted into a forearm vein in your non-dominant arm by a qualified and experienced person. As a result, you only need to be poked once. An initial blood sample is taken. In total, blood will be drawn 6 times. All in all, about 60 ml of blood is drawn per session.



3. MRI: You will be led into the MRI room and given earplugs to protect you from the scanner noise (this noise is only there during the scans, not all the time). We will also make sure that your head is slightly fixed by placing pillows on the sides and we put a pillow under your knees so that you lie comfortably. A small tube is placed between your lips, similar to a straw, so that you can drink. For the stomach scans, a coil will be placed on your abdomen. In the MRI scanner, you communicate with the researchers via an intercom. You will also receive an alarm bell in case you need to urgently speak to the researchers. Through a mirror, you will see a TV screen at the back of the scanner. If you have to wear glasses, we will provide you with glasses that can be used in the MRI. You will be asked about your appetite, well-being and thirst.

4. Now the first scans of your brain and stomach will be made (20 min). After that, you will drink a first sip of the drink and assess its sweetness and pleasantness. We will ask you about this over the intercom. Then you will drink the rest (500 ml in total).
5. After drinking, the scans of your brain and stomach will be repeated several times for ~60 min. We will also ask you to re-score your appetite, well-being and thirst and take 5 more blood samples. In total, you will spend about 80 minutes in the MRI machine. Between scans, you can listen to the radio. Researchers supervise the scanning from the control room and regularly check that you are doing well over the intercom.

5. What is expected of you?

For the experiments to go well, you will need to follow these agreements:

- do not participate in any other medical-scientific research
- follow instructions
- come to all test sessions on time

It is also important that you contact the coordinating investigator in these situations:

- Before you start taking (new) medication. Even if these are homeopathic medicines, natural medicines, vitamins, and/or over the counter medicines.
- If you become pregnant
- If you are hospitalised or treated in a hospital
- If you suddenly experience health issues
- If you no longer want to participate in the study
- If your contact information changes

6. What side effects, adverse effects or inconveniences can you experience?

Side effects of test products

In this study, you will receive water and flavored water sweetened with different sweeteners or table sugar. These products are safe to consume and no side effects are expected.

Measurements

Participating in MRI research is safe but can be a bit uncomfortable because you must lie still in the MRI machine during the scans and spend in total approximately 80 minutes in the machine Your head is slightly fixed in the main coil. This can feel a little uncomfortable. The MRI machine makes a lot of noise during scanning, but we will reduce this noise for you by giving you earplugs. If you are not comfortable in narrow spaces, such as the tunnel of the MRI machine, we recommend that you do not participate.

Placing the cannula may temporarily hurt or cause localized bruising. It is also possible that the placement does not succeed in one go, in which case we will try again. This will always take place in consultation; if you don't want us to try a second time, we will not this. You can withdraw from the study at any time. It may also happen that the cannula is no longer running properly and that no more blood can be drawn. In that case we decide, in consultation with you, whether a new cannula will be placed. However, this only happens sporadically. All in all, we take 60 ml of blood from you per session. For adults, this amount is no problem. For comparison: 500 ml of blood is taken for a blood donation at the blood bank.

7. What are the possible advantages or disadvantages of participating in this study?

Participating in the study can have advantages and disadvantages. Below we list them.
Think about these carefully, and talk about them with others. You will not benefit from participating in this study yourself, but your participation will help the researchers to better understand how different sweeteners affect the brain and body. In return for your participation, you will receive a financial compensation.

Participating in the study may have the following disadvantages:
o You will have to spend time to attend the screening session (30 min) and the six testing sessions (10 hours total)
o You will have to come to the testing sessions sober (overnight fasting).
o You may be uncomfortable during the measurements
o You must follow the instructions and agree to the terms of the study

8. When does the research stop?

The researcher will let you know if there is any new information about the study that is important to you. The researcher then asks you if you will continue to participate.

In these situations, the study stops for you:
- All visits, as described in section 4 of this document, have been completed
- For women: you have become pregnant.
- You want to stop the study yourself. You may do so at any time. Please report this immediately to the investigator. You do not have to say why you are stopping.
- The investigator thinks it is better for you to stop.
- One of the following bodies decides that the research should stop:
  - o Wageningen University
  - o The government
  - o The Medical Ethical Review Committee reviewing the research

What happens if you stop the research?
The researchers use the data and body material (blood samples) collected up to the time of stopping. If you wish, collected body material can be destroyed. Please communicate this to the researcher.

The study officially ends when all participants finish all their test sessions.

9. What happens after the study?

Will you receive the results of the study?
If you want to know about the main results of the study, the researchers will inform you after all the data has been processed and analysed. This is expected to happen no later than 9 months after the end of the study.

10. What do we do with your data and body material?

Are you participating in the study? Then you also give permission for your data and bodily material to be collected, used and stored.

What data do we store?
We store the following data:
- your name
- your gender
- your address
- your date of birth
- data about your health.
- data we collect during the study.

During the study, images of your brain and stomach and your subjective assessments are collected.

What body material do we store?
We store tubes of blood.

Why do we collect, use and store your data and body material?
We collect, use and store your data and body material to answer the questions of this study. And to publish the results.

How do we protect your privacy?
To protect your privacy, we code your data and your bodily material. We only put this code on all your data and body material. The key of this code will be kept in a secure location at the university. When we process your data and body material, we always use only that code. Even in reports and publications about the research no one can recall that it was about you.

Who can see your data?

Some people can see your name and other personal data without a code. These are persons who check whether the researchers are conducting the research properly and reliably.

These individuals can access your data:

- Members of the committee monitoring the security of the study.
- National and international supervisory authorities. For example, the Inspectorate of Health Care and Youth.

These persons will keep your data confidential. We ask you to give permission for this access.

How long do we keep your data and bodily material?

We keep your data at the university for up to 15 years after the end of the study. We keep your body material at the university until the research is published. After that we destroy your body material.

May we use your data for other research?

Your data may also be relevant to other scientific research of the brain. To this end, your data, such as a brain scan may be shared in a scientific database. On the consent form you indicate whether you give permission for this. Do you not give your consent? Then you can still participate in this research.

What happens in case of unexpected discoveries?

The MRI scans taken are not intended and are not specifically designed for finding abnormalities. If the researchers discover a possible abnormality, they will consult a radiologist for further verification of the scan. If the radiologist thinks the finding may be of importance to your health, you and your general practitioner will be informed and you may be referred for further investigation.

In case of abnormal blood sugar and insulin levels, the research physician will be consulted and, if necessary, you and your general practitioner will be informed. The chance of finding something abnormal in healthy volunteers is relatively small. If you do not wish to be informed of such chance findings, you may not participate in this study.

Can you withdraw your consent to the use of your data?

You can withdraw your consent to the use of your data at any time. But please note: Do you withdraw your consent, and then researchers have already collected data for a study? Then they may still use this data. As for your body material, the researchers will destroy it after you withdraw your consent. But have measurements already been performed with your body material? Then the researcher may continue to use them.

Would you like to know more about your privacy?

- Would you like to know more about your rights when processing personal data? Then go to www.autoriteitpersoonsgegevens.nl/en.
    - Do you have questions about your rights? Or do you have a complaint about the processing of your personal data? If so, please contact the person responsible for the processing of your personal data. For your research, this is the principal investigator. See Appendix A for contact information.
- If you have complaints about the processing of your personal data, we encourage you to first discuss them with the research team. You can also go to the Officer Data Protection Officer of Wageningen University (see Appendix A). Or you can file a complaint to the Dutch Data Protection Authority.

Where can you find more information about the study?

You can find more information about the study on the following website: www.ClinicalTrials.gov. After the survey, the website may show a summary of the results of this survey. You can find the investigation by searching on the registration number NCT05575687 or through this link.

11. Will you receive a payment if you participate in the study?

You will receive a payment of €300 after completing all study sessions (6 in total) according to the reimbursements for research from the Department of Human Nutrition and Health. This amount includes any travel expenses. If you come to the test sessions by car, you will receive an exit ticket for the parking lot.

If you decide to stop participating in the study, you will receive the amount of the total reimbursement in proportion to the number of testing sessions you attended. The compensation for taking part in this study is declared to the Tax and Customs Administration as income.

12. Are you insured during the study?

Insurance has been arranged for everyone participating in this study. The insurance will pay for damages caused by the study. But not for all damages. In appendix B you will find more information about the insurance and the exceptions. It also tells you who you can report damages to.

13. Will my doctor be informed about my participation?

You cannot participate in the study if you do not have a general practitioner. The general practitioner will only be informed if we come across unexpected discoveries relevant to your health.

14. Do you have any questions?

If you have any questions, please talk to the research team. If you would like advice about the participation in this study, please talk with the independent expert (Dr. J. Nikken). He knows about the study but is not directly involved.
Do you have a complaint? Then discuss this with the researcher. Would you rather not discuss this with the researcher? Then go to the complaints officer (Eveline Waterham). All contact details can be found in Appendix A.

15. How do you consent to the study?

You can first think about participating in this research. Then you will tell the researcher if you understand the information and whether or not you want to participate. Do you want to participate? Send us an e-mail and you will be invited to an information meeting. There we will tell you more about the study and you can ask questions. If you then wish to participate, you will be invited to a screening session. There you will fill out the consent form that you will find enclosed with this information letter. You and the researcher will both receive a signed version of this consent form.

Thank you for your time.

16. Appendices:

A. Contact Information
B. Insurance Information
C. Consent Form

Appendix A: Contact information

Coordinating and Principal investigator:

Dr. Paul Smeets
Wageningen University - Division of Human Nutrition and Health
Telephone: +31 317 484681 (mobile)
Email: paul.smeets@wur.nl

Research physician:

Myrte Naaktgeboren, general physician
Wageningen University - Division of Human Nutrition and Health
E-mail: myrthe.naaktgeboren@wur.nl

Independent expert:

Dr. J. Nikken, radiologist
Hospital Gelderse Vallei
E-mail: NikkenJ@zgv.nl

Complaints:

Eveline Waterham
Wageningen University - Division of Human Nutrition and Health
E-mail: Eveline.waterham@wur.nl

Privacy:

Officer of personal data Wageningen University & Research
Mr. WFEM (Frans) Pingen
E-mail: privacy@wur.nl:

Appendix B: Insurance Information

Wageningen University has taken out insurance for everyone participating in this study. The insurance covers damage resulting from participation in the study. This applies to damage incurred during the study or within four years after the end of your participation in the study. You must have reported damage to the insurer within these four years.

The insurance does not cover all damage. The bottom of this text explains briefly what damage is not covered.

These provisions are in the Medical Research Involving Human Subjects Act. This decree is on www.ccmo.nl, the website of the Central Committee on Research Involving Human Subjects (see 'Library' and then 'Laws and regulations').

In the event of damage, you can contact the insurer directly.

The insurer of the study is:	
Name:	HDI Global SE
Address:	Postbus 925, 3000 AX Rotterdam
Telephone:	+31(0)10 40 36 100
E-mail:	www.hdi.global
Policy number:	V-055-862-396-3 / V0100109572

The insurance provides coverage up to a maximum of € 650,000 per participant and a maximum of € 5,000,000 for the entire study. Here, a maximum of € 7,500,000 applies to all research at Wageningen UR per insurance year.

The **insurance will not cover the following** damage:

- Damage due to a risk about which you were informed in the written information. This does not apply if the risk is more serious than anticipated or if the risk was very unlikely;
- Damage to your health that would also have occurred if you had not taken part in the study;
- Damage due to not (completely) following directions or instructions;
- Damage to your offspring, due to a negative effect of the study on you or your offspring;
- Damage from an existing treatment method in research on existing treatment methods.

Appendix C: Consent form

- I have read the information brochure. I was able to ask questions. My questions were answered to my satisfaction. I had enough time to decide whether to participate.
- I know that participation is voluntary. I also know that I may decide at any time not to participate after all or to withdraw from the study. I do not need to give a reason for this.
- I know that for the purposes of monitoring the study, some people will be able to see my information. Those people are listed in this information letter. I give these people permission to see my data for audit
- I give the researchers permission to collect and use my data to answer the research questions of this study and related questions that can give deeper insight in the topic under investigation.
- I know that data about me that is significant to this study will be used for scientific purposes and possibly published. This includes the possibility that the MRI images may be shared in an online database for further scientific analysis. I agree to this, provided that my privacy is guaranteed.
- I know that the MRI images collected in this study are not suitable nor intended for diagnosis
- I give consent to give me and my doctor or specialist information about accidental discoveries made during the study that are important for my health.
- For women: I know that I should not get pregnant during the study. In case I do get pregnant, I must withdraw from the study.
- I give permission for my data to be kept for 15 years after this study.
- I want to participate in this study.

Name of study participant:	Date:

Signature:

- I declare that I have fully informed this study participant about this study.
- If any information becomes known during the study that could influence the participant's consent, I will inform him/her of this in a timely fashion.

Name of investigator:	Date:

Signature:

The participant will receive a full information brochure and a signed copy of this consent form.