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What we want to achieve with our study: We will use this study to examine how the brain circuits involved in processing signals from our body, such as those relating to our breathing perceptions, depend on aspects of our psychology, such as our levels of anxiety.	2-3
What we would like you to know: Hereby we want to invite you to participate in our basic science study. We are looking for healthy women and men aged 18 to 40 years. You will receive detailed information about all inclusion and exclusion criteria via e-mail and during the telephone pre-screening.	
What participating in the study means for you: Study design: Basic Research Study Overview: • Online pre-screening questionnaires, duration approx. 15 mins • Laboratory testing and practice session, duration approx. 2 hours • Magnetic resonance imaging (MRI) experiment, duration approx. 2 hours.	3-5
The benefits and possible risks for you within the study: We would like to inform you that you do not stand to gain direct personal benefits from participation in this experiment. Study participation supports basic science research and you will receive a monetary compensation for expenses. The methods involved are associated with only very small risks.	5
What rights you have, if you participate in the study: You are free to decide whether you want to participate in this study or not. If you decide now you wish to take part, you can at any time withdraw from the study. You do not have to provide reason or justification for your withdrawal. During the study we will collect data about you. If you cancel your study participation, the data up to the point of withdrawal may still be used.	4
What are the obligations associated with participation in the study: If you choose to take part, you must follow certain rules for your own safety.	5
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What you confirm with your consent: In addition to this summary, extensive additional information can be found on the following pages. These are an integral part of the information. With the signing of the declaration of consent you accept the complete document.	2-9
Who to contact: At any time you can contact the following project leader to answer any questions: Name: Dr. Olivia Faull Function:project leader Address: Translational Neuromodeling Unit, Wilfriedstrasse 6, 8032 Zurich, Switzerland Phone number: Tel. 044 634 91 11, email: faull@biomed.ee.ethz.ch	7

Title of the study:
"High-resolution functional magnetic resonance imaging of interoception of breathing"

Sponsor:
Prof. Dr. med. Klaas Enno Stephan, PhD, Translational Neuromodeling Unit (TNU), Institute for Biomedical Engineering, University of Zurich and the ETH Zurich, Wilfried Strasse 6, 8032 Zurich

Dear Sir or Madam,

We are employees of the Translational Neuromodeling Unit and would like to ask whether you wish to take part in a study with us.

1) Objectives of the study

In this study we will examine how the brain circuits involved in processing signals from our body, such as those relating to our breathing perceptions, depend on aspects of our psychology, such as our levels of anxiety.

2) Selection of the persons to participate in the study

We wish to find healthy volunteers (male and female) aged between 18 and 40 years. There are specific inclusion and exclusion criteria, which can be queried at the time of screening by the university registration office for study participants (UZH & ETH) as well as directly before study participation.

3) General study information

Background and purpose of the study:
In this project we want to understand the neurobiological mechanisms for the recognition and perception of internal body signals (such as perception of breathing). In particular, we are interested in how psychological properties, such as different levels of anxiety, interact with the brain circuitry involved in this perception. To investigate this, we use high-resolution magnetic resonance imaging.

Study design: Basic research

Location:
The study will be conducted at the Translational Neuromodeling Unit, Wilfriedstrasse 6, 8032 Zurich, and at the magnetic resonance center at the University Hospital Zurich, Rämistrasse 100, 8091 Zurich.

What is magnetic resonance imaging?
Magnetic resonance (abbreviation "MR") or magnetic resonance imaging (abbreviation "MRI") is an imaging procedure. It generates images from inside the body, to help us study the structure and function of organs and tissues. For the imaging procedure, the person to be examined is placed in a strong magnetic field, which is generated by a machine shaped like a type of tube. During the course of the investigation, the device creates additional magnetic fields that are very much weaker than the main magnetic field. The switching of these additional fields can is noticable by knocking and humming noises that can achieve a volume of up to 60 decibels. The device also uses radio waves similar to those used by radios and mobile phones. The various fields are combined to encourage the hydrogen atoms in the body to create a resonance signal. This signal is received by highly sensitive antennas, and powerful computers then put together a picture. In contrast to x-ray examinations or investigations with a computer tomograph (CT), MRI uses no radioactive radiation.

The study duration and total number of volunteers: The study should be completed by August 2020.
A total of 70 volunteers are expected to be included.

The implementation of the study follows the corresponding regulations (laws) in Switzerland.
In addition, we observe all internationally recognized guidelines. The study has been checked and approved by the competent Cantonal Ethics Commission.

4) Sequence of participation

Participation in the study includes an initial online screening that involves questionnaires measuring your general levels of anxiety. Prior to inclusion in the study, we will kindly ask you to complete these online questionnaires measuring anxiety (as a personality trait, that every human shows in a different manifestation). We are looking to recruit healthy men and womend within the normal spectrum of anxiety with no history of diagnosed psychiatric conditions. If you are selected for the study, this is followed by one laboratory practice session and one MRI experiment on two different days.

About the laboratory examination:

- The laboratory examination takes place in the Translational Neuromodeling Unit (TNU), Wilfriedstrasse 6, 8032 Zürich.
- You will firstly be asked to complete a range of questionnaires to measure various aspects of your psychology and personality, and re-check your safety for MRI scanning.
- We will then measure how sensitive you are to very small changes in your breathing, where you will breathe through a mouthpiece connected a non-invasive breathing system. We will ask you to rate whether or not you could observe a change in the resistance to your breathing, and how confident you are of that perception. The duration of this task will be approximately 30-60 minutes.
- Lastly, we will test your lung function and run a practice session for the MRI scan. Here, you will first breathe through a hand-held device to test aspects of your lung function. We will then set you up to comfortably breathe through a different, non-invasive breathing system that will be used during the MRI experiment. We will regularly ask you to rate your breathing using a button box, and it may change to become mildly harder or easier to breath at times. At the end, we may ask you to fill in a questionnaire relating to the breathing task you performed. The duration of this task will be approximately 30-60 minutes.
- The breathing system can be easily removed without assistance if at any point you become uncomfortable, or would like to take it off. You will be able to breathe at all points – there are no occlusions in the breathing task. In addition, measures such as your heart rate, breathing rate and expired gases may be monitored and recorded.
- The duration of the total experimental session will be approximately 3 hours.

About the MRI examination:

- The experiment takes place in the Magnetic Resonance Centre at the University Hospital Zurich, Rämistrasse 100, 8091 Zurich.
- Important: Please note that due to the strong magnetic field no metallic or magnetic material can be brought to the MRI cabin. For this reason please take off all metallic objects in the waiting area. Do not forget to remove for example earrings, belts, metallic objects on your clothes, pens in your pockets, keys, coins etc. Data storage devices (e.g. credit cards) and all metallic items on your body (e.g. jewellery, piercings, necklaces, earclips, hairclips etc.) also have to be removed. In contrast, dental fillings are no problem.
- To ensure that no metallic item can be missed, you will be asked to take of your street clothes. The staff will provide you with examination cloth. Changing rooms are available on site.
- For the experiment you will be positioned comfortable on the examination table and driven inside the tubular MRI scanner. The overall duration will be approximately 90 minutes in the scanner.
- At the beginning of the experiment you will be fitted with a breathing system, exactly the same as in the practice session in the laboratory. You will be able to remove the breathing system at any point should it become uncomfortable. Once the breathing task is over you will be able to remove the breathing system for the rest of the scan.
- You will receive hearing protection from the MRI operator.
- During the experiment we ask you to stay relaxed and calm.
- During the measurements, we will ask you not to move the head as far as possible and not to speak to avoid movement of facial muscles. However, if necessary, you can at any point communicate via the intercom, and scanning can be immediately stopped by pressing the

emergency button.

- During the breathing task, you will be presented with stimuli (such as shapes on the screen) as well as small changes in your breathing, similar to the practice session the day before. You will also be asked to rate your breathing using a button box, and your responses will be recorded. In addition, measures such as your heart rate, breathing rate and expired gases will be monitored and recorded. The duration of the scanning experiment will be approximately 60 minutes.
- The duration of the total experimental session will be approximately 2.5 hours.
- We will offer you financial compensation for expensesat the end of the experiment.

Note before both experiments (see also point 6 "obligations of the participating"):

- In the 24 hours prior to the study experiment you will be required to consume no alcohol.
- If you should fall ill shortly before the experiment (even if you do not deem it seriously ill, e.g. a cold), we would ask you to please contact the experimenter immediately, so that we may evaluate whether participation is possible or useful.
- In the 7 days prior to the study experiment you will be asked to refrain from taking any medicines.
- If a medication is still necessary, please contact the project manager and detail the drug name. Together with the medical head of th TNU it will be decided whether the study date needs to be moved.
- Please bring to the study experiment a valid ID card (identity card or driving license).
- For those who wear contact lenses: During the experiment, contact lenses will need to be removed. Please bring along a contact lenses container and solution if needed, and your reading glasses should you need them.
- All metallic items on the body (Body piercing / jewellery) must be removed for the MRI.

For women of childbearing age (“Not in menopause yet and last menstruation less than 12 month ago, not surgically sterilized, ovaries and/or uterus not surgically removed”) participating in the experiment: For security reasons we have to ask whether a pregnancy might be possible. In case of any doubt, participation is only possible when a mandatory pregnancy test has been carried out.

Directions/arrival to MRI-center of the USZ by tram:
From Zurich main train station by tram 10 (direction Oerlikon/airport) or tram 6 (in the direction of Zoo) to the stop ETH/University Hospital. From Bellevue, with Tram 9 (direction Hirzenbach) also to the stop ETH/University Hospital. The University Hospital is well visible from the stop. The main entrance of the university hospital is located opposite the main entrance of the ETH. In front of the university hospital is a golden statue. Enter the university hospital at the main entrance. Follow the aisle straight to the end where you will see three purple elevators on the right hand side, and travel 2 floors down into the floor V. From the elevator the signs to the MR-Center are well visible. Follow the signs for the MR-Center and go right twice until you are at the end of a slightly downward corridor, where you will find the entrance to the MR-Center. With the accessible phone you can use the internal numbers (59573) to indicate your arrival. The project leader will then collect you from the reception area. The MRI will take place in Room "MR V 25".

5) Rights

Only take part in this study if you wish to participate on your own free will. No one should in any way push or persuade you to take part – the decision is entirely up to you. You do not need to justify why you do not wish to take part. If you decide to participate, you are free to withdraw at any time. You also do not need to justify your withdrawal, or provide any reason for your discontinuation with the study. To withdraw, please contact the person at the end of this study information.

6) Obligations

If you decide to participate in the study, you must observe certain rules. These rules are necessary for your health and safety. We will be there to support you as well as we can throughout the experiment. As a study participant you are obliged to:

- Follow the instructions of your investigator and the study plan (see "Note before the experiment" in the study process, point 4 above)

7) Benefits for participating

We would like to note that there are no direct personal benefits from participation in this experiment. Study participation supports basic research.

8) Risks

In compliance with safety regulations, particularly regarding electronic implants and metallic parts at or in the body and close to the magnet, there are no risks associated for you. It is therefore important that you carefully complete the "MRI safety questionnaire". The responsible person will be happy to assist you with this.
Magnetic resonance imaging is a non-invasive procedure that has been regularly used in hospitals for many years for routine diagnostics and in research, without any negative health consequences. You should avoid rapid movements in the magnetic field; in rare cases there may be slight nerve irritation and associated minor temporary dizziness or a metallic taste in the mouth. Few people also report perceiving short light pulses, so-called phosphenes. For the radio waves used in this study, wave limits are similar to those of mobile phone use and they are strictly adhered to during MRI examinations. In this way, any heating of the body is avoided. For protection against the knocking sound during the course of the investigation, you will receive hearing protection. During the scanning procedures, the investigator is situated in the adjacent room. You can communicate with the investigator at any time via the intercom system.
For an improved reconstruction of MR images during the experiment, we measure the magnetic fields in the scanner. This is done with the so-called "field probes" which are placed outside of the head coil in the scanner. These field probes are not certified for medical applications, but are developed for research purposes. They do not touch or affect your body in any way but simply serve to measure the magnetic field generated by the scanner. The MR scanner itself has a stronger magnetic field than those used in clinical MRI Devices (7 Tesla instead of 1.5 or 3 Tesla). For this reason it is used only as a research tool, and not for medical applications (Diagnostics).

The behavioral tasks offer no apparent risks. At all times during the investigation you will be able to contact and communicate with the investigator.

According to present knowledge, magnetic resonance imaging is considered as safe method of examination. However, at present data is lacking to rule out any hidden risk for the unborn life during pregnancy.
The concers regarding the use of MRI in early pregnancy are based on the consideration that static and changing magnetic fields in the radio frequency range might warm up the fetal tissue, which is especially vulnerable in the phase of organogenesis, and could be damaged as a result. Moreover, is remains unclear what consequences the high level of noise during the examination could have on the foetus. For these reasons you can unfortunantely not participate in our study when you are pregnant.

9) Results from the study

The project leader will inform you of all new knowledge generated from the study that you have participated. You will receive information orally and in writing.
The methods used in this study are not suitable for use in clinical diagnostics. However, it may happen that an abnormality is detected. In the case of such an incidental random finding, you can chose in advance whether we:

a) Share the results with you (and on request a doctor of your choice)
b) Do not inform you of the results
c) Share the results with a person of your choice (for example a relative, your family doctor etc.) Please enter the name and contact data, and your choice on the declaration of consent, which is located at the end of this document.

10) Data confidentiality

In this study we collect personal and medical data (so-called health-related personal data). This data will be encrypted, i.e. labelled with a code. This code does not give any indication about you, and the code list is kept locked within the TNU. During the study only the study staff and the TNU database administrators, and after the study only the TNU database administrators will have access to the code list.
It may be that the authorities which pre-checked and approved the study, or the institution which is funding the study, may verify that all rules are respected during the execution of the study. This is also done for your safety. For such controls, the head of the study may need to disclose your personal and medical data to authorities. In the case of any reported damage, a representative of the insurance may be required to view your data. However, insight is limited to the data that would be required in order to deal with the case of damage.

All persons involved in the study in any way are required to act with absolute confidentiality. We will not publish your name in any report or publication, in print or on the Internet.

11) Further use of your data

You can withdraw from the study at any time, without providing any information on your reasons for doing so. We will evaluate the data acquired up until that point, but we will keep your data anonymous, i.e. we will permanently delete your name. It would be impossible for anyone to learn whom the data came from.
We will keep your recorded data within the TNU in an encrypted form for further research purposes, and also for use by third parties, provided you have given permission for this. However, you have the right to reject any further use of your data or, if you have given the permission once, to withdraw it at any time without providing reasons for doing so. For more information, please contact someone from the study team.
Your consent (or refusal) for further use of the data is independent of the study participation. This means that you can also take part in this study, even if you do not agree to further use of your data.
You have the right to refuse your consent for this further use of data at any time or, if given once, to withdraw it at any time without the need to provide any reason for doing so. In this case, data collected up to that point cannot be used by third parties and will only be accessible to the study team in unencrypted form.
In the framework of scientific cooperation with external partners or when providing data for scientific review (e.g. required from scientific journals during publication process), we will only pass on encrypted, non-genetic health-related personal data, i.e. the recipient cannot know at any time where the data originated from. Your name will never be published in the internet or a publication. Prior to the publication of a scientific study some scientific journals require to store the collected data of all participants in databases accessible for other researchers, so that control analyses could potentially be conducted. In case we are doing so, the data will always be encrypted and it is therefore impossible for anyone track it back to you. All persons having access to your data within the study are required to act with absolute confidentiality. We comply with all rules for data protection, and you as a participant are entitled to have access to your data at any time.

12) Compensation

If you take part in this study, you will receive the following compensation for expenses: For the pre-screening no expense allowance is provided. However, for a subsequent participation the actual study, an expense allowance will be paid.
Participation in the actual experiment is in total CHF 180.- compensated for both session together (approx. 6 hours). You will also receive CHF 10.- for the completion of the online questionnaires after the pre-screening. Expenses (e.g. travel expenses) will not be reimbursed.
If you withdraw from the study, you will be compensated for the total number of hours in which you participated.
Your participation will not lead to any costs for you or your health insurance.

13) Liability

If you incur any damage to your health as a result of the study, the liability falls to the institution responsible for carrying out the study. This liability applies if it can be proved that the damage was due to the study experiment. The Translational Neuromodeling Unit has, through the Department of Finance of the Canton of Zurich an insurance policy with the Zurich insurance group, to cover this liability in case of damage.
If you have suffered a damage, please contact the project leader (see contact information).

14) Financing of the study

This study is funded by core funding from the University Zurich and ETH Zurich for the Translational Neuromodeling Unit (Prof. K.E. Stephan).

15) Contact person(s)

For any confusion, worries or emergencies, during the study or thereafter, you can contact the project leader at any time.

Project leader:

Dr. Olivia Faull
Translational Neuromodeling Unit (TNU)
Institute for Biomedical Engineering
University of Zurich and ETH Zurich
Wilfriedstrasse 6
8032 Zurich
Phone: 044 634 91 36
Email: faull@biomed.ee.ethz.ch

Written declaration of consent for study participation

- Please read this form carefully
- Please ask if you do not understand anything or would like more information

Study number:	BASEC-NR.: 2017-02330
Title of the study	**"High-resolution functional magnetic resonance imaging of interoception of breathing"**
Responsible institution (sponsor) (full address)	Prof. Dr. med. Klaas Enno Stephan, PhD Translational Neuromodeling Unit Institute for Biomedical Engineering University of Zurich and the ETH Zurich Wilfriedstrasse 6, 8032 Zurich
Place of execution:	Dr. Olivia Faull Translational Neuromodeling Unit Wilfriedstrasse 6, 8032 Zurich & Magnetic Resonance Center University Hospital Zurich Rämistr. 100, 8091 Zurich
Study investigator: Name and surname (in block letters)	Dr. Olivia Faull
Study participant: Name and surname (in block letters) Date of birth: Gender	…….. …….. ☐ Male ☐ Female

- I have been informed by the signing study staff member (orally and in writing) of the purpose, the procedure of the study, the likely effects, the possible advantages and disadvantages, and any possible risks involved with participating in the study.
- All of my questions regarding participation in the study have been answered satisfactorily. I can keep the written study information and will retain a copy of my written declaration of consent. I accept the content of the written study information I received regarding the above mentioned study.
- I am taking part in this study on my own free will. I can at any time, and without reason, withdraw my consent to participate without any disadvantage to me.
- I have had enough time to consider my decision.
- I have been informed that an insurance policy will cover any damage if I can prove that the damage incurred as a result of the study.
- If any incidental findings should occur in this study:
  a) ☐ I would like to be informed. If you would like us to also inform a doctor of your choice, please enter the name and contact information here:
  ……..
  b) ☐ I would not like to be informed.
  c) ☐ I would like the decision to be left to the following person (name and contact):
  (☐ Mentioned above)
  ……..
- I understand that my health-related and personal data can be passed on,in encrypted form only, for research purposes of this project.

- I agree with the futher use of my personal data for research in unencrypted form (see item 11 in the participant information sheet): ☐ Yes ☐ No
- I agree that the competent experts of the study sponsor, the authorities and the Cantonal Ethics Commission are allowed to inspect my original data for review and control purposes, but under strict observance of confidentiality.
- I am aware that the participant obligations listed in the study information are to be observed throughout the study. In the interest of my health, the investigator of the study can at any time exclude me from the study.
- I confirm that all my information provided during the study participation is correct.

Place, Date	Signature of the study participant

Confirmation by study staff member:

I hereby confirm that I have described and explained the essence, meaning and scope of the study to this participant. I assure to fulfill all obligations with regards to this study in accordance with the law as it now stands. If I should at any time during the implementation of the study learn information that could influence the willingness of the participant to participate in the study, I will inform him/her immediately.

	Name and surname of the study staff member (in block letters) ……
Place, Date	Signature of the study staff member