Anfrage zur Teilnahme an medizinischer Forschung:

Predicting individual fatigue levels based on brain connectivity – Pilot Study (QFMRI)

Dear study participant

We are asking you here if you would be willing to participate in our research project.

Your participation is voluntary. All data collected in this research project is subject to strict data protection regulations.

The research project will be conducted by Prof. Dr. med. Klaas Enno Stephan and Dr. Sandra Iglesias, Translational Neuromodeling Unit (TNU) der Universität und ETH Zürich. If you are interested, we would be happy to provide you with information about the results of this research project.

We will explain the most important points to you and answer your questions. So that you can already get an idea, here is the most important information in advance. Further, more detailed information will follow.

Why do we carry out this research project?

- In this study we would like to test and optimise new cognitive tasks centred on the evaluation and experience of fatigue (a chronic state of exhaustion). Furthermore, we would like to understand how subjectively perceived fatigue levels are associated with the functional connectivity strength in the brain. To this end, we will perform fMRI measurements.

What does praticipating in this research project mean for you?

- Type of participation: Participation in the study includes filling in of questionnaires and one magnetic resonance imaging (MRI) session.
- Participation overview: If you decide to participate in our study, you will be asked to complete an online pre-screening from home (approx. 30 minutes). If you are selected for the study, this is followed by online questionnaires that you can fill in from home (ca. 1 h 25 min: Informed consent and questionnaires) and one MRI appointment (approx. 3 h) at the University Hospital Zurich.

What are the benefits and risks associated with participation in this study?

Benefits

- You have no direct benefit by participating in this research project.
- By participating in the research project, you support basic research.

Risk and burden

- The methods used are only associated with extremely low risks.

With your signature at the end of this document, you confirm you are participating voluntarily and that you have understood the contents of the entire document.

Detailed information

1. Objectives and Selection

If you decide to participate in this research project, you are a *participating person*. Volunteers aged 18 or older can participate in this study. There are specific inclusion and exclusion criteria, that are queried at the time of the screening, as well as directly before starting with the measurements.

In this study we would like to test and optimise new cognitive tasks centred on the evaluation and experience of fatigue. Furthermore, we would like to understand how subjectively perceived fatigue levels are associated with the functional connectivity strength in the brain. To this end, we will perform fMRI measurements. This is a pre-study for a later study in which we will investigate in patients the subjective evaluation and experience of fatigue and its association with functional connectivity.

2. General Information

- The study will be conducted at the Magnetic Resonance Center at the University Hospital Zurich, Rämistrasse 100, 8091 Zurich (MRI measurement).
- Participation in the study includes filling in questionnaires and one magnetic resonance imaging (MRI) session.
- The study lasts for three years (until approx. 01/2026). A total of 115 volunteers (100 participants and 15 pilot data sets) are expected to be included in this study.
- The implementation of the study follows the corresponding regulations (laws) in Switzerland. In addition, we follow all internationally recognized guidelines. The study has been checked and approved by the Cantonal Ethics Committee.

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 tube. During the course of the investigation, the device creates additional magnetic fields that are very much weaker than the main magnetic field surrounding us. The switching of these additional fields is noticeable by the knocking and humming noises that can achieve a volume of up to 100 decibels (the noise can be reduced strongly by using ear protection). 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 is combined to an image by powerful computers. In contrast to x-ray examinations or investigations with a computer tomograph (CT), MRI uses no radioactive radiation.

3. Participation Procedure

Participation in the study includes an initial online screening that involves questions about the inclusion and exclusion criteria and a questionnaire measuring fatigue. If you are eligible to participate in the study, this is followed by online questionnaires that you can fill in at home and one MRI measurement at the University Hospital Zurich.

<u>To note before the study appointment (see also point 5 “Duties"):</u>

- If you should fall ill shortly before the study appointment (even if you do not consider to be seriously ill, e.g. a cold), we would ask you to please contact the experimenter immediately, so that we may evaluate whether participation is reasonable or possible.
- Please, do not drink alcohol within 24 hours before the study appointment.
- Please refrain from taking any pain killers or other medication within 48 hours before the study appointment.

- Should a medication intake still be necessary, please contact the investigator and tell him the name of the medicine you are taking. Together with the medical team of the Translational Neuromodeling Unit (TNU) it will then be decided whether the study date needs to be postponed or whether a study participation is unfortunately not possible.
- Please, do not consume cannabis within 14 days before the study appointment.
- Please bring a valid ID card (e.g. identity card or student ID) to the study appointment.

Additional points to note before the MRI-measurement:

- For contact lens wearers: During the measurement, lenses must be removed. Therefore, please bring a contact lens case, contact lens solution, and if necessary your reading glasses with you.
- All metallic items on the body (jewellery/ piercings) must be removed for the MRI.
- For safety reasons, we have to ask 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"*) about a possible pregnancy. If you are unsure about this, participation can only take place if a pregnancy test is carried out and if this test is negative. Please, drink a glass of water before the measurement to be able to perform this test.

Directions to the MR-center of the USZ by tram:

From Zurich main train station use tram 10 (direction Oerlikon/airport) or tram 6 (direction Zoo) to the stop ETH/University Hospital. From Bellevue use 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 to 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 floor V. From the elevator the signs to the MR-center are well visible. Follow the signs for the MR-center and turn 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 publicly available phone you can call the internal number (59573) to indicate your arrival. The experimenter will then collect you from the reception area.

About the online pre-screening:

- You will be asked to give your consent for the screening of the inclusion and exclusion criteria. To that end, you will be asked to answer questions such that these criteria and inclusion and exclusion criteria regarding the participation in MRI-studies can be evaluated.
- Additionally, you will be asked to fill in an online questionnaire to assess fatigue. Please note, that our study design is not suitable to make medical diagnosis.
- Based on the results of these questionnaires we will evaluate whether a participation in this study is possible.

About the online questionnaires:

You will be asked to provide your consent to participate in this part of the study. Thereof, you will be asked to fill in questionnaires on your psychological well-being, on your demographics and you will be asked to write down situations during or after which you experienced the strongest fatigue. These questionnaires will be filled in online (approx. 1 h 25 minutes).

About the 3T MRI appointment:

- The appointment takes place in the Magnetic Resonance Centre at the University Hospital Zurich, Rämistrasse 100, 8091 Zurich.
- First, we will check the inclusion and exclusion criteria, the duties and for your safety the MR-inclusion and exclusion criteria (MR safety questionnaire). Female participants will be asked whether a pregnancy might be possible. If you are unsure, a pregnancy test needs to be performed before the MR measurement and must be negative.
- Subsequently, you will be asked to fill in questionnaires regarding your sleepiness and your usual sleeping habits and to summarise the fatigue situations previously written down.
- You will receive special clothes for the MR examination. Lockers for your own clothes and changing rooms are available on site.
- It is important, that all personal items (e.g. wallet, credit cards etc.) and metallic objects (e.g. piercings, necklace, earrings, hair clips etc.) are removed from your body and are safely stored in the lockers.
- For the MR measurement you will be comfortably positioned on the scanner bed and you will be moved inside the tubular MRI scanner. The overall duration of the MR examination will be approximately 65 minutes.
- You will receive hearing protection from the experimenter.
- During the measurements, we ask you to be as relaxed and calm as possible, not to move your head, not to speak, and also not to move your facial muscles if possible. If necessary, however, you can contact the experimenter at any time via intercom. You can also stop the measurement at any time by pressing an emergency button.
- During the MRI tasks, you will be presented with questions and instructions on the screen. We will record your answers as well as your heart rate and breathing and monitor them accordingly. In addition, we will monitor you via a camera. The real-time video only serves monitoring purposes and will not be recorded or saved.
- The total duration of this session is approx. 3 h, including a break outside the MRI scheduled after the first half of the measurement
- The financial compensation for your participation will be paid to you at the end of the study.

We may have to exclude you from the research project prematurely. This can happen if you are unable to follow the study instructions or if you unexpectedly become unwell during the visit.

4. Benefit

You will not personally benefit from your participation. With your participation in the study, you will support basic research.

5. Voluntariness and Obligations

You are participating voluntarily. If you do not wish to participate in this research project or if you wish to withdraw your participation at a later timepoint, you do not have to give any reasons for this.

If you are participating in this research project, it is necessary that you adhere to the specifications and requirements of the study described in the research protocol.

These rules are necessary for your health and safety. During the study, we will support you in this as much as possible. Furthermore, you are obliged to follow the instructions of the experimenter and to adhere to the research protocol (see «To note before the study appointment», point 3 «Participation Procedure»).

6. Risks and Burdens

According to current knowledge, MRI examinations are without health risks. There are only with regard to metal parts or electronic implants in the body known risks. In addition, the MR measurement can cause claustrophobia or discomfort due to the confined space. It is therefore

important that you fill in the "MR safety questionnaire" conscientiously. The staff in charge will be happy to assist you.

MRI devices have been routinely used in hospitals for diagnostic purposes for many years without any negative consequences for health. Please avoid sudden movements within the magnetic field; in rare cases this may cause slight nerve irritation and associated slight temporary dizziness or metallic taste in the mouth. Few people report brief light perceptions, so-called phosphenes. For the radio waves used in this study, the upper limits are set similar to those of mobile phones and these are strictly adhered to during MRI examinations. In this way, heating of the body is avoided. You will be given hearing protection to protect you from the tapping noise during the examination. During the measurement, the person conducting the examination is in the adjacent room. You can communicate with the experimenter at any time via the intercom system.

According to current knowledge, magnetic resonance imaging is considered a safe examination method. However, there is currently not enough data available to rule out hidden risks to the unborn child during pregnancy.

The reservations about the use of an MRI in early pregnancy are based on the fear that due to the static magnetic fields and the changing magnetic fields in the radiofrequency range, the fetal tissue, which is particularly sensitive in the phase of organogenesis, could be heated and thus damaged. It is also unclear what consequences the high noise level during the examination has for the unborn child. At present, it is therefore recommended to avoid MRI examinations during pregnancy.

For these reasons, you will unfortunately not be able to take part in the study if you are pregnant and you will be asked on the day of the MR-measurement whether pregnancy is possible. If you are unsure, a pregnancy test is mandatory before the MR-measurement.

The behavioural tasks do not involve any risks. During the MR-measurement, you can contact and communicate with the experimenter at any time.

7. Results

There are:

1. individual results of the research project that affect you directly,
2. individual results of the research project, which are discovered unintentionally (so-called incidental findings)

pt 1: During the course of the project the experimenter will inform you about any new results and findings that are important for you personally. You will be informed verbally and in writing and you can then decide again whether you want to continue participating in the project.

pt 2: Incidental findings are unexpected findings that are not directly related to the research project and that have been discovered by chance.
The methods used in this study are not suitable for clinical diagnostics. Nevertheless, it can happen that an incidental finding is detected in MR images and/or questionnaire responses. In the case of such incidental findings, or if the analysis of your data could contribute to the prevention, detection or treatment of existing or anticipated future diseases, you can choose in advance whether we should:

a) inform you of the results (and, at your request, a doctor of your choice);
b) not inform you about the results;
c) inform a person of your choice about the results (for example relatives, your doctor, etc.).

Please fill in the name and contact details, as well as your choice on the informed consent form, which can be found at the end of this document.

8. Confidentiality of data

8.1 Data processing and encoding

For this research project, data about your person and health will be collected and processed, partly in automated form. During data collection your data will be encrypted. Encryption means that all reference data that could identify you (name, date of birth, etc.) is deleted and replaced by a code. People who do not have access to this key list cannot draw any conclusions about you. The key list is always kept password-protected under lock and key at the Translational Neuromodeling Unit (TNU) University Zurich & ETH Zurich. Those people who do not know the key can therefore not draw any conclusions about your person.
In the case of a publication, the data is therefore also not traceable to you as an individual. Your name will never appear on the internet or in a publication.
Increasingly, there is a requirement from scientific journals and government research funding organisations that when research results are published, the individual data (so-called raw data) must be submitted, made accessible or shared. If we meet this requirements, then the data is always encrypted and therefore also not traceable to you as a person. The study personnel and the TNU database administrators who have access to your data are bound by professional secrecy. The requirements of data protection are complied with at all times and you, as a participant, have the right to inspect your data at any time.

If data is sent abroad, stored there and analysed for this project (without further use): The data is sent encrypted, examined there for this project and archived for 10 years. Only persons or institutions authorised by the TNU have access to this encryption. The institution abroad has equivalent standards to the institution in Switzerland. The authorised person/institution that ensures equivalent data protection abroad is responsible for compliance with national and international data protection guidelines.

Very few professionals will see your unencrypted data, and only to carry out tasks within the research project. These persons are subject to professional confidentiality. As a participant, you have the right to access your data. Possibly this project will be reviewed by the Cantonal Ethics Committee or by the institution that initiated the project. The project leader may need to disclose your personal and medical data for such audits/ inspections. Likewise, in exceptional cases, a representative of the insurance company may also need to look at your data. However, this inspection is limited to the data that is absolutely necessary to deal with a very unlikely claim. All persons involved must maintain absolute confidentiality.

8.2 Data protection

All data protection specifications are strictly adhered to. It is possible that your data may need to be transmitted in encrypted form, for example for publication, and may be made available to other researchers. If health-related data is stored on site, it constitutes a database for research purposes. Data will be archived in encrypted form as part of this project in a database for research purposes for at least ten years.

8.3 Data protection in case of further use

Your data could be used for answering other questions at a later date at the Translational Neuromodeling Unit, University of Zurich & ETH Zurich and/or could later be transferred to another database in Switzerland or abroad and used for as yet undefined research (further use). This other database must comply with the same standards as the database for this project.

The re-use of data is important to us because scientific journals and government research funding organisations increasingly require that when research results are published, the data must be made freely available to other researchers.

For this further use, we ask you to sign another consent form at the very end of this document. This second consent is independent of your participation in this project.

9. Rights of access during inspections

This research project may be reviewed by the Cantonal Ethics Committee. The project management must then disclose your data for such checks. All persons involved must maintain absolute confidentiality.

10. Withdrawal

You can withdraw from the research project at any time if you wish, without giving a reason. In this case, however, the data collected up to that point will still be stored and evaluated in encrypted form. Please check that you agree with this before participating in the project.

You also have the right to withdraw your consent to the further use of your data at any time without giving reasons. In the context of collaborations with external scientific partners, only encrypted, non-genetic, health-related personal data is passed on, i.e. the recipient cannot know that the data originates from you.

11. Compensation

If you have completed the screening, you can win a voucher from "WISHCARD" worth CHF 100 .-, with a draw taking place after every 100 study participants.

If you subsequently participate in this research project, you will receive compensation for this in the amount of CHF 90.-. Expenses (e.g. travel expenses) are not reimbursed.

If you withdraw from the study, you will receive compensation for the number of hours you have participated in.

There are no costs for you or your health insurance for participating.

12. Liability

In the unlikely event that you suffer damage as a result of the project, the institution responsible for carrying out the project is liable. This liability applies if it can be proven that the damage is due to the study. The Translational Neuromodeling Unit is covered by an insurance policy taken out by the Finance Department of the canton of Zurich at «Zürich-Versicherung», to cover liability in the event of damage. If you have suffered damage, please contact the project leader (see contact details).

13. Funding

The research project is supported by research funds of University Zurich and ETH Zurich for the Translational Neuromodeling Unit (Prof. K.E. Stephan).

14. Contact person(s)

You may ask questions about project participation at any time. Also, if you have any uncertainties that arise during the research project or afterwards, please contact:

Project Leader:
Dr. Sandra Iglesias, PhD
Translational Neuromodeling Unit (TNU)
Institute for Biomedical Engineering
University of Zurich and ETH Zurich
Wilfriedstrasse 6, 8032 Zürich
Phone: 044 634 91 23,
Email: qfmri@ethz.ch

Informed Consent

Written declaration of consent to participate in a research project
Please read this form carefully. Please ask if there is anything you do not understand or would like to know. Your written consent is required for participation.

BASEC-Number (after submission):	2022-02308
Title of research project (scientific and lay language):	**Predicting individual fatigue levels based on brain connectivity – Pilot Study** (Acronym: QFMRI)
Responsible institution (Project management with address):	Translational Neuromodeling Unit Institut für Biomedizinische Technik Universität Zürich und ETH Zürich Wilfriedstrasse 6, 8032 Zürich
Place of execution:	Translational Neuromodeling Unit Institut für Biomedizinische Technik Universität Zürich und ETH Zürich Wilfriedstrasse 6, 8032 Zürich Magnetresonanzzentrum Universitätsspital Zürich Rämistr. 100, 8091 Zürich
Project Leader of the research project at the study site	Dr. Sandra Iglesias, PhD
Participating person: **Name und surname (in print letters):**	……..……
Date of birth:	D D . M M . Y Y Y Y
Gender:	☐ male ☐ female ☐ diverse

- I have been informed orally and in writing by the undersigned experimenter of the trial or by the investigator about the purpose, the procedure of the research project, about possible advantages and disadvantages as well as about possible risks.
- I am voluntarily participating in this research project and accept the content of the written study information provided on the above research project. I have had sufficient time to make my decision.
- My questions in relation to the participation in this research project have been answered. I keep the written study information and receive a copy of my written consent form.
- I agree that the responsible experts of the project and the Ethics Committee in charge of this research project may inspect my unencrypted data for testing and control purposes, but in strict compliance with confidentiality.

- In the case of incidental findings in the course of this study that directly affect my health:

  a) ☐ I want to be informed in any case. If you wish that we additionally inform a doctor of your choice, please enter the name and contact details here:

  ……

  b) ☐ I do not want to be informed.

  c) ☐ I would like to leave the decision to the following person (name incl. contact details):

  (☐ above-mentioned)

  ……

- I know that my health-related and personal data can only be passed on in encrypted form for research purposes for this research project (also abroad). The sponsor guarantees that data protection in accordance with Swiss standards will be maintained.
- I can withdraw from participation at any time and without giving reasons. The data collected up to that point will still be used for analyses of the research project.
- I am informed that an insurance policy covers damages resulting from the research project.
- I am aware that I must comply with the obligations stated in the information document. In the interest of my health, the experimenter or the project leader may exclude me at any time.
- I confirm that all the information I provide during my participation in the study is correct.

Place: …… Date: D D . M M . Y Y Y Y	Signature participating person ……

Confirmation of the experimenter: I hereby confirm that I have explained the nature, significance and scope of the research project to this participant. I assure that I will fulfil all obligations in connection with this research project in accordance with the law applicable in Switzerland. If, in the course of the research project, I learn of aspects that could influence the readiness of the participating person to take part in the research project, I will inform him/her immediately.

Place: …… Date: D D . M M . Y Y Y Y	Name und surname of the experimenter (in print letters) …… Signature of the experimenter

Informed consent for further use of data of the participating person

Name und surname (in print letters):	……..……
Date of birth:	D D . M M . Y Y Y Y
Gender:	☐ male ☐ female ☐ diverse

I give permission that my encrypted data from this research project be further used for research. To this end, we will store the data collected in encrypted form in scientific databases - as increasingly required by scientific organisations and journals – or share the encrypted data with other researchers under data protection conditions (Data Use Agreements) so that it can be used for future research projects. This consent is valid indefinitely.

I understand that the data is encrypted and the key is kept secure. The data can be sent to other databases for analysis at national and international level if they adhere to the same standards as in Switzerland. All legal requirements for data protection are complied with.

I decide voluntarily and can withdraw this decision at any time. If I withdraw, my data will remain encrypted, as the data would otherwise lose its value for future research projects. I only inform the project leader and do not have to justify this decision.

Usually, all the data is evaluated as a whole and the results are published in summary form. If there is a result that is important for my health, it is possible that I will be contacted. If I do not wish to be contacted, I will inform the project leader.

I give my permission that my data be anonymised and I understand that in this case I can neither be informed about random results nor withdraw from the research project.

If results from the data are commercialised, I have no claim to a share of the commercial use.

Place: …… Date: D D . M M . Y Y Y Y	Signature participating person ……

Confirmation by the experimenter: I hereby confirm that I have explained to this participant the nature, significance and scope of the further use of data.

Place: …… Date: D D . M M . Y Y Y Y	Surname and name of experimenter (in print letters) …… Signature of the experimenter