Information letter for the research study:

Non-invasive brain stimulation for schizophrenia patients with auditory hallucinations (Main experiment)

Background and purpose
This is an invitation to take part in a research study that aims to investigate whether weak electrical stimulation of the brain can help you to better cope with hearing voices/sounds that are not real. Such hallucinations often occur in schizophrenia, but current treatments (for example medication) do not always work or have unwanted side-effects. The aim of this study is therefore to find better treatment options for individuals who are distressed by voices/sounds and where other treatments are insufficient.

What is going to happen in the study?
The study comprises five days of electrical stimulation. The stimulation does not hurt, but you can experience a tingling, itching sensation at the skull (for more information, please sea chapter A below), Three days before and on the last day of stimulation, you will be asked a few questions about the voices/sounds that you hear (ca. 60 min); carry out a few tasks that assess concentration and learning (ca. 15 min); and neuroimaging in the form of magnetic resonance imaging (MRI, ca. 60 min). We also want to obtain relevant health information from your journal.
In addition, we ask you to take part in a follow-up examination where we repeat the assessment (interview about voices, concentration and learning tasks, MRI) three months after the stimulation. You will be given an iPod for the entire period between stimulation and follow-up examination to assess changes in your hallucinations/voices every day. We also ask you for permission to contact you at a later stage to invite to further studies in case this becomes relevant.

Possible advantages and disadvantages
The stimulation may reduce distressing sounds/voices that you experience. Brain stimulation and MRI can feel uncomfortable to some people but are regarded as safe. For more information regarding potential risks, please see chapter A below. To examine whether the stimulation works, half of the participants are going to receive fake "sham" stimulation: the electrodes are attached to the skull but the electric current is switched off. You are randomly assigned to the group that gets "real" or to the group with sham stimulation. In case you got "sham" stimulation will you have the possibility to get the real stimulation at the end of the study.

What happens to your data and personal information about you?
The data and personal information that is collected can only be used in accordance with the aim and purpose of the study. All personal information and data will NOT contain your name, personal ID, or other directly identifiable information. An anonymous code that you can find on this informed consent will be used for all personal information and data that we collect about you. Only authorized staff working on this project have access to the informed consent that can be used to identify you. It will not be possible to identify you when the findings of this study are published. The informed consent and other questionnaires, and thus the only possibility to identify you, will be destroyed after the project is over on 31.03.2020.

Voluntary participation
Your participation is entirely voluntary. At any point and without providing reasons you can withdraw your consent from this study. This will not have consequences for your further treatment. If you wish to take part, you sign the informed consent on the final page. If you want to withdraw consent or have questions regarding the study, you can contact:
Marco Hirnstein, phone: 55 58 60 62, e-mail: marco.hirnstein@uib.no

Chapter A: Further information about brain stimulation, neuroimaging, and the general procedure

What kind of brain stimulation is used and how long will it take?
The brain stimulation method is called tDCS (transcranial Direct Current Stimulation). It consists of a weak electric current that passes through two electrodes attached to your skull. The current is so weak that you typically experience only a tingling, perhaps slightly itchy sensation.
You will receive tDCS for five days. Every day you receive tDCS twice for 20 min with a break of 3 hours between the two stimulations.

How is the effect of tDCS assessed?
Voices/sounds: Before, during, and after tDCS, we will ask you questions about the voices/sounds that you hear. You will also get an iPod to report how you feel about those voices/sounds on a daily basis.
Neuroimaging (MRI): Three days before, on the last day of tDCS, and three months after tDCS, we would like to examine your brain with MRI. MRI is based on a magnetic field and no radioactivity. You lie on a bench that is driven into the MRI-machines magnetic field. During MRI you will hear some noise, which is coming from the MRI-machine and absolutely normal.
You will be asked to carry out an attention task while you are in the MRI-machine. The whole procedure takes a bit more than one hour.
Daily functioning and mental capacity: Neuropsychological tasks will be carried out to test your daily functioning and, for example, your ability to concentrate, thinking, and learning new things. This will also be done three days before, on the last day of tDCS, and three months after tDCS.

Who can take part?
To prevent complications, people who answer «yes» to any of the following questions may not be able to take part in the study. In this case we will discuss further with you and your treating physician:

- Do you have metal devices in your body (e.g., heart pacemaker, metal artificial hip, electrodes)?
- Do you have metal splinters in your eyes or other parts of your body?
- Did you undergo surgery of the brain, eyes, or heart?
- Are you pregnant?
- Do you have claustrophonia?
- Have you or your parents/siblings had an epileptic seizure?
- Do you have major skin diseases (e.g., neurodermatitis) at your skull?
- Have you had any of the following conditions: Head trauma, broken skull, brain surgery, stroke, meningitis, or brain tumour?

Your medical record will be checked for any condition that could prevent participation in the study. We will also obtain relevant information from your journal at the Haukeland University hospital and other hospitals where you have been treated.

Possible distress and risk factors
The examinations are usually complication free if all answers above are answered with ”no”. As far as we know, there are no risks or side-effects of combined MRI/tDCS examinations, if you follow the safety protocols and instructions. Tattoos and makeup can in some cases cause skin irritations. Dental braces are normally unproblematic but can affect the quality of MRI images. If you have dental braces, please check with the MRI staff/radiogaphers.
As far as tDCS is concerned are no negative longterm effects known to date. In people at risk of epilepsy tDCS can trigger an epileptic seizure. Therefore people who have had an epileptic seizure are

not allowed to take part in this study. In some cases headaches, skin irritation, and nausea have been reported when tDCS was applied with high electrical currents. In our study, however, will tDCS not exceed 2mA, which is in line with international safety standards. Antipsychotic medication can reduce the threshold and thus increase the risk for an epileptic seizure, but to date there have been no reports of seizures with the setings that are used in this study.

Discovery of incidental findings in the MRI examination
MRI is primarily used in research and to date not an appropriate method for clinical psychiatric diagnose. The staff that carries out the MRI examination is typically not trained in radiological diagnostic. All MRI images, however, will be checked routinely by a trained physician/neuroradiologist. If something is discovered that could be an illness, the medical staff will contact you and ask you whether you wish to have further examinations and/or be formally transferred to the respective medical department at the Haukeland University hospital or another hospital.

What do you need to be careful with?
The use of alcohol and drugs can increase the risk for an epileptic seizure when you are being stimulated with tDCS. During the five day stimulation period we therefore encourage **you to NOT use alcohol or drugs**.
Metal pieces that get into the MRI magnetic field can lead to injuries. Therefore, you need to remove the following items before your go into the room with the MRI-machine:

- Watches, glasses, ear rings, and other jewellery
- Bank cards with magnet stripes
- Metal pieces on clothing (e.g., belts)
- Coins, pens, keys and other metal pieces (e.g., hair pins)
- Dental braces
- Hearing devices, cochlear implants

What is going to happen? And why?
The study is carried out at the Helse Bergen Sandviken Clinique and at the Radiology department at the Haukeland University hospital. On the first day the following happens: You will be asked a few questions regarding the voices/sounds that you hear. You will complete a few tasks to assess your ability to concentrate, learn, and think. You will undergo an MRI examination.
The next five working days you will receive tDCS, twice a day.
On the last of those five days the same last tDCS session, you will undergo the same assessment (including MRI) as on day one.
In addition, you undergo questions, tasks, and MRI three months later.

Compensation for participation
You will receive a compensation of 600 NOK for taking part in this study.

Chapter B: Further information about personal data, funding, and insurance

Personal data
The personal data about you that is going to be stored is obtained from the examinations and tasks described in chapter A. You also give us permission to obtain relevant health information from your treating physician/therapist, the Haukeland university hospital, and other health facilities where you have been treated before. All your data will be de-identified and only authorized staff will have access to the anonymous code that links you to your data (see above). Everybody with access to your health data is bound to medical confidentiality. The department of biological and medical psychology is responsible for handling the data. When the project ends on 31.03.2020 will the informed consent and all

other study materials that contain your name be destroyed or deleted, making it impossible to identify you.

Sharing anonymous data with other researchers
If you agree to participate in the study, you also allow us to share the anonymous data with external researchers in the future.

Right to access and delete personal information
If you agree to participate in the study, you have the right to see what personal information is stored. You also have the right to correct errors in your personal information If you withdraw your consent from the study, you can demand to delete personal information unless they have already been used in analyses or scientific publications.

Funding
The study is financed by the University of Bergen and the Bergen Research Foundation.

Insurance and financing
Normal patient insurance rules apply.

Information about the study outcome
You have the right to receive information about the outcome of the study. For information about provisional or final results please contact:
Marco Hirnstein, phone: 55 58 60 62, email: marco.hirnstein@uib.no).

Consent to take part in study

Participant: I would like to participate in the study (name, date)

_____

Experimenter: I hereby confirm that I have informed the participant about the study (name, date)

_____

Anonymous code:_____