Accelerated Deep Transcranial Magnetic Stimulation for Smoking Cessation

Lead Principal Investigator: Bernard Le Foll

Informed Consent Form

Project ID: 5240

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Summary of Informed Consent Form

Study Title: *Accelerated Deep Transcranial Magnetic Stimulation for Smoking Cessation*

Below is a summary of information about the study. There is more information in the document called an "informed consent form" that follows this summary. Please read the informed consent form. The research team will also talk to you about the study and you can ask any questions you may have.

Participation in research is voluntary. It is your choice whether you take part in this clinical trial.

STUDY PURPOSE
The purpose of this trial is to find out whether a form of non-invasive brain stimulation, called accelerated transcranial magnetic stimulation (aTMS), can help people stop smoking. We are testing how well this treatment works and how safe and acceptable it is for people who want to quit smoking.

DURATION
It is expected that study participation will last about 6 months. Participants will be followed for approximately 26 weeks, including one week of treatment and several follow-up visits afterward.

STUDY PROCEDURES
This study is looking at how accelerated deep brain stimulation (aTMS) help people quit smoking. Participants will attend study visits at Week 1 (for treatment) and at Weeks 3, 5, 9, 13, and 26, during which researchers will ask questions, collect urine samples, and perform safety checks. You will be asked to attend a 5-day treatment period in Week 1, with four sessions per day that may take up to 3 hours each day.

RISKS.
Participation in this study may involve risks to you. These risks are described in detail in the informed consent form.

The risks you are most likely to experience are:
- Mild headaches (about 1 in 4 people)
- Scalp discomfort during or after treatment (about 1 in 10 people)
- Fatigue (less than 1 in 10 people)

The most serious risks are:
- Seizure, which is very rare (less than 1 in 10,000 people)

BENEFITS.
We do not know if you will receive medical benefit from participation but researchers hope that this study will fulfil its purpose and benefit others in future.

ALTERNATIVES.
You do not have to participate in this study to receive medical care. You may have other medical options – you should discuss this with your health care provider.

Informed Consent Form for Participation in a Research Study

Study Title: *Accelerated Deep Transcranial Magnetic Stimulation for Smoking Cessation*

Study Doctor: *insert name, department and telephone or pager number*

Sponsor/Funder(s):
Bernard Le Foll
Waypoint Centre for Mental Health Care
Sunnybrook Research Institute

Emergency Contact Number (24 hours / 7 days a week): _____

Non-Emergency contact numbers are noted at the end of this document under the section heading "Contacts".

INTRODUCTION

You are being invited to participate in a clinical trial (a type of study that involves research). You are invited to participate in this trial because you are an adult who smokes cigarettes and is interested in quitting. This consent form provides you with information to help you make an informed choice. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to participate in this research study.

Please take your time in making your decision. You may find it helpful to discuss it with your friends and family.

Taking part in this study is voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive outside the study.

IS THERE A CONFLICT OF INTEREST?

Describe any conflict of interest that exists or may appear to exist as it relates to any of the investigators, study staff or member of their immediate family. A conflict of interest exists if there is a potential benefit to the investigator(s), study staff or member of their immediate family beyond the professional benefit from academic achievement or presentation of the results. Examples include, but are not limited to, speaker's fees, travel assistance, consultant fees, honoraria, gifts, and intellectual property rights such as patents. A declaration of conflict of interest should include the identity of the person with the conflict of interest, the type of incentive or inducement, and its source. See examples below.

There are no conflicts of interest to declare related to this study.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Each participating site must ensure that the standard or usual treatment described in below matches the standard of care at that site. Site specific differences must be reflected in the Centre Initial Application and the site-specific consent form.

The standard or usual treatment for people who want to quit smoking includes medications such as nicotine replacement therapy (NRT), varenicline, or bupropion, along with behavioral counseling. While these treatments can be helpful, not everyone benefits from them.

Accelerated deep transcranial magnetic stimulation (aTMS) is a new type of brain stimulation therapy being explored for smoking cessation. aTMS has been studied and used for treating depression for several years, but it has not yet been widely tested for addiction. This study aims to explore how acceptable, safe, and feasible aTMS is for people who want to stop smoking.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to find out whether a type of brain stimulation called accelerated deep transcranial magnetic stimulation (aTMS) is a safe, acceptable, and practical treatment for helping people quit smoking. aTMS is already approved and used for depression, but this study is looking at how it might help with smoking addiction. The study is focused on evaluating the feasibility and early signs of effectiveness of this treatment.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study in order to receive treatment or care. Other options (in addition to the treatment described above) may include, but are not limited to:

- Nicotine replacement therapy (such as patches, gum, lozenges, or inhalers)
- Prescription medications like varenicline (Champix®) or bupropion (Zyban®)
- Self-help materials

Please talk to your usual doctor or the study doctor about the known benefits and risks of these other options before you decide to take part in this study. Your usual doctor or the study doctor can also discuss with you what will happen if you decide not to undertake any treatment at this time.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that about 40 people will take part in this study, from research sites located in Ontario.

This study should take about 2 years to complete, and the results should be known in about 2.5 years.

WHAT WILL HAPPEN DURING THIS STUDY?

ASSIGNMENT TO A GROUP

This is a one-arm study, which means that everyone who joins will be assigned to the same group. All participants will receive the same treatment, and there is no comparison or control group in this study.

Once a certain number of participants have entered the intervention phase of the study from all of the research sites combined, no more participants will be enrolled into the study at any site. It is possible that you may finish the screening phase and be ready to enter the intervention phase of the study, but not be enrolled into the study.

WHAT IS THE STUDY INTERVENTION?

If you agree to take part in this study, you will receive a type of brain stimulation called accelerated deep transcranial magnetic stimulation (aTMS). This involves wearing a helmet-like device that delivers magnetic pulses to specific areas of your brain involved in craving and self-control.

The treatment will take place over 5 consecutive days. Each day, you will receive four short sessions of stimulation, each lasting about 18 minutes, with breaks of at least 30 minutes between sessions. You will be at the hospital for about 3 hours each treatment day.

The procedure is non-invasive, does not require medication, and you will be awake during the sessions.

WHAT ELSE DO I NEED TO KNOW ABOUT THE STUDY INTERVENTION?

If you have side effects while you are on this study, the study doctor may make changes to the intervention.

There are several approved approaches for quitting smoking, including behavioral counseling and medications. In this study, you will receive a behavioral counseling component alongside the brain stimulation treatment. However, if you decide to take part, you may not be able to use other treatments—such as medications like varenicline (Champix®), bupropion (Zyban®), or nicotine replacement products (e.g., patches or gum)—during the treatment and follow-up phase.

WHAT ARE THE STUDY PROCEDURES?

Non-Experimental Procedures

The following tests and procedures will be done as part of this study. Some of these may be part of your standard care, in which case the results may be used. Some may be done more frequently than if you were not taking part in this study, and some may be done only for the purpose of the study. If the results show that you are not able to continue participating, the study doctor(s) will let you know.

- Questionnaires – You will be asked to complete several questionnaires about your smoking behavior, mood, cravings, and other related health information.
- Urine tests – These will be used to check for recent smoking and substance use.
- Safety monitoring – You will be monitored for side effects, including physical exams and review of any health changes.
- Behavioral counseling – You will participate in brief behavioral counseling sessions, which are designed to support your efforts to quit smoking and help you stay motivated throughout the study.

Experimental Procedures

The following test is considered experimental and will only be done for participants in this study:

- Accelerated deep transcranial magnetic stimulation (aTMS) – This is a non-invasive brain stimulation procedure that uses magnetic pulses to stimulate areas of the brain linked to smoking behavior. You will receive this treatment four times per day for five days, with each session lasting about 18 minutes.

QUESTIONNAIRES

You will be provided with several questionnaires before starting the study and again during follow-up visits over the course of 6 months. The purpose of these questionnaires is to understand how the brain stimulation affects your smoking behavior, mood, cravings, and overall mental well-being. Each set of questionnaires will take about 10–20 minutes to complete.

The information you provide is for research purposes only. Some questions may be personal, and you can choose not to answer any questions that make you uncomfortable.

Some questionnaire responses—such as items related to suicidal thoughts—will be reviewed by the study team to help ensure your safety. If you report any concerns in these areas, the study doctor or research staff may follow up with you.

MANDATORY SAMPLE COLLECTION

The researchers doing this study need to collect urine samples to check for recent smoking, use of other addictive substances, and pregnancy (if applicable), as part of the study.

These samples are a necessary part of the research and will not be sold. Once testing is complete, any leftover urine will be safely disposed of. Reports from these tests will be shared with the study doctor(s). If you would like to know your test results, you may ask the study team.

Urine collection

Urine will be collected at several time points throughout the study, including before treatment begins and during follow-up visits. Testing will be done using a point-of-care dip test at the study site, with results available quickly. The remaining urine will not be stored or sent to another laboratory and will be discarded after testing.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you choose to participate in this study, you will be expected to:

- Tell the study doctor or researchers about your current medical conditions;
- Tell the study doctor or researchers about all prescription and non-prescription medications and supplements;
- Tell the study doctor if you are thinking about participating in another research study;
- Tell the study doctor if you become pregnant or father a child while participating in this study;
- Avoid drinking alcohol or using unregulated substances during the treatment week, and follow instructions from the study team during the follow-up period;
- Do not start any new medications for quitting smoking during the study, including nicotine replacement therapy (NRT), varenicline, or bupropion, unless discussed with the study doctor.

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The study intervention will last for 5 consecutive days. During this time, you will receive four short sessions of brain stimulation (aTMS) each day.

You will be asked to come back to the clinic for follow-up visits approximately 2 weeks, 4 weeks, 8 weeks, 12 weeks, and 26 weeks after the treatment ends. These visits help us monitor your progress, assess safety, and evaluate the effects of the intervention.

You may be seen more often if the study doctor decides it is necessary for your safety or care.

Even if you stop the treatment early, we would still like to keep track of your health for about 6 months to understand the longer-term effects of participating in this study. We would do this by asking you to return to the clinic for scheduled follow-up visits or by calling you to see how you are doing.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff.

You may be asked questions about your experience with the study intervention.

You may withdraw your permission to use information that was collected about you for this study at any time by letting the study doctor know. However, this would also mean that you withdraw from the study.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The study doctor may stop your participation in the study early, and without your consent, for reasons such as:

- You are unable to tolerate the study intervention (deep TMS)
- You start taking other treatments for smoking cessation that could interfere with the study
- New information shows that the study intervention is no longer in your best interest
- The study doctor no longer feels that participating in the study is the best option for you
- You become pregnant or plan to become pregnant during the study
- The Sponsor decides to stop the study
- The Research Ethics Board, or other regulatory authorities withdraw permission for the study to continue

If this happens, it may mean that you would not receive the study intervention for the full period described in this consent form.

If you are removed from this study, the study doctor will discuss the reasons with you.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be others that are unexpected. You should discuss any concerns with the study doctor.

The study doctor will monitor you closely for any side effects. When possible, other medications, such as pain relievers for headaches, will be provided to help make side effects less serious and more manageable. Many side effects go away shortly after the study intervention is stopped. However, in rare cases—such as a seizure—side effects may be serious. Both of our recruitment sites, Waypoint and Sunnybrook, have the capacity to manage such events promptly.

Risks and side effects related to the experimental intervention, accelerated deep transcranial magnetic stimulation (aTMS), which we are studying, include:

Very likely (21% -100%):

- **Headache**: Often mild and located around the stimulation site. Typically occurs during or shortly after treatment and usually goes away within an hour or with common pain relievers.
- **Scalp discomfort or pain**: A tingling or tapping sensation at the site of stimulation. This usually becomes less noticeable with repeated sessions.

Less likely (5 – 20%):

- **Fatigue**: Feeling tired after treatment.
- **Dizziness or light-headedness**: May occur during or shortly after treatment. Usually resolves quickly.
- **Mood changes or irritability**: Some participants may notice temporary changes in mood, such as feeling more irritable or anxious.
- **Muscle twitching in the face or jaw**: Caused by stimulation of nearby nerves, usually mild and short-lasting.

Rarely (1 – 4%):

- **Mania or hypomania**: In people with bipolar disorder or underlying mood instability, stimulation may trigger increased energy, reduced need for sleep, or elevated mood. You will be monitored for these symptoms.
- **Seizure**: Although extremely rare (estimated risk of 0.0023% per session in prior studies), there is a small risk of experiencing a seizure. You will be screened to reduce this risk, and staff are trained to manage this situation if it occurs.

WHAT ARE THE REPRODUCTIVE RISKS?

The effects that accelerated deep transcranial magnetic stimulation (aTMS) may have on an unborn baby (fetus) are unknown. Although aTMS has generally been considered safe for pregnant people based on clinical experience and retrospective case reports, most studies—including this one—exclude people who are pregnant to ensure safety.

If you are able to become pregnant, you must not become pregnant while participating in this

study. If you are unsure whether your current birth control method is reliable, please speak to the study doctor or research team.

If you become pregnant at any time during the study, you must tell the study doctor immediately. The study doctor will ask whether you are willing to share information about your pregnancy as part of the study. If you agree, this information will help us understand whether there are any risks to pregnancy from the study intervention. If you prefer not to share this information, or if you change your mind later, you may withdraw your consent at any time without providing a reason. This will not affect your participation in the study, and it will not impact your health care in any way.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

You may or may not benefit from participating in this study. The expected benefit from taking part in this study is a potential reduction or cessation of cigarette smoking. The type of brain stimulation used in this study—deep transcranial magnetic stimulation (deep TMS)—has been approved by Health Canada for smoking cessation in adults. Therefore, participants may experience similar benefits, such as decreased craving and improved ability to quit smoking.

Although we cannot guarantee that every participant will benefit, previous research suggests that this treatment may help reduce smoking and prevent relapse.

We also hope that the information learned from this study will help improve smoking cessation treatments for other people with tobacco use disorder in the future.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

Note: *If there will be disclosure of personal identifiers, i.e., disclosed on any research-related information/documents including samples or scans, or as part of the unique identifier, these disclosures must be justified in the REB application and approved. Please ensure that you are aware of institutional and REB policies with respect to the disclosure of personal identifiers.*

If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study.

Records identifying you will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines.

- Waypoint Centre for Mental Health Care, one of the study sites and the Sponsor of this study
- Sunnybrook Research Institute, one of the study sites and the Sponsor of this study
- The research ethics board who oversees the ethical conduct of this study in Ontario
- This institution and affiliated sites, to oversee the conduct of research at this location

Information that is collected about you for the study (called study data) may also be sent to the organizations listed above. Representatives of Clinical Trials Ontario, a not-for-profit organization, may see study data that is sent to the research ethics board for this study. Your name, address, email, or other information that may directly identify you will not be used. The records received by these organizations may contain your disclose identifiers e.g., participant code, initials, sex, and date of birth.

Communication via e-mail is not absolutely secure. We do not recommend that you communicate sensitive personal information via e-mail.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be used in analyses and will be published/ presented to the scientific community at meetings and in journals. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of the study intervention.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

A copy of the consent form that you sign to enter the study may be included in your health record/hospital chart.

Can my study data be used for other research?

There are no plans for use of your study data in other research.

WILL FAMILY DOCTORS/HEALTH CARE PROVIDERS KNOW WHO IS PARTICIPATING IN THIS STUDY?

Your family doctor/health care provider will not be informed by the study team that you are taking part in the study. You can choose to let your family doctor/health care provider know, if you like.

WILL INFORMATION ABOUT THIS STUDY BE AVAILABLE ONLINE?

A description of this clinical trial will be available on http://www.clinicaltrials.gov. This website will not include information that can identify you. You can search this website at any time.

WHAT IS THE COST TO PARTICIPANTS?

The accelerated deep transcranial magnetic stimulation will be supplied at no charge while you take part in this study.

You may not be able to receive the study intervention after your participation in the study is completed. There are several possible reasons for this, some of which are:

- The intervention may not turn out to be effective or safe.
- Your caregivers may not feel it is the best option for you.
- You may decide it is too expensive and insurance coverage may not be available.
- The intervention, even if approved in Canada, may not be available free of charge.

The study doctor will talk to you about your options.

Taking part in this study may result in added costs to you. For example:

- There may be costs associated with hospital visits. For example, parking or transportation, or snacks/meals during your stay.
- You may miss work as a result of participation in this study.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

Each participating site must ensure that the information below matches the compensation/reimbursement provided at that site. Site specific differences must be reflected in the Centre Initial Application and the site-specific consent form.

Yes. If you decide to participate in this study, you will receive a total of $550 if you complete all study visits and procedures.

This amount includes:

- $25 for completing the screening visit
- $25 for completing the baseline visit
- $250 for attending all five days of the accelerated TMS treatment sessions ($50 per day)
- $50 for each of the five follow-up visits (Week 3, 5, 9, 13, and 26)

In the case of research-related side effects or injury, you will be referred for appropriate medical care.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

You have the right to be informed of the results of this study once the entire study is complete. If you would like to be informed of the results of this study, please contact the study doctor. The results of this study will be available on the clinical trial registry (see the “Will information about this study be available online” section for more details).

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the study doctor or involved institutions for compensation, nor does this form relieve the study doctor or their agents of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to participating in this study.

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to your study doctor, or the doctor who is in charge of the study at this institution. That person is:

_____	_____
Name	Telephone

If you have questions about your rights as a participant or about ethical issues related to this study, you can talk to someone who is not involved in the study at all. That is the Research Ethics Board(REB). REB is a group of people responsible for the ethical oversight of this study.

__ Sunnybrook Research Ethics Board _	__416-480-6100 x 88144__
Name	Telephone

SIGNATURES

- All of my questions have been answered,
- I understand the information within this informed consent form,
- I allow access to medical records and related personal health information as explained in this consent form,
- I do not give up any legal rights by signing this consent form,
- I agree to take part in this study.

Signature of Participant	PRINTED NAME	Date

Signature of Person Conducting the Consent Discussion	PRINTED NAME & ROLE	Date

The following attestation must be provided if the participant is unable to read or requires an oral translation:

If the participant is assisted during the consent process, please check the relevant box and complete the signature space below:

☐ The person signing below acted as an interpreter, and attests that the study as set out in the consent form was accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and additional discussion arising from this process.

PRINT NAME of Interpreter	Signature	Date

Language

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to the participant, and any questions have been answered.

PRINT NAME of witness	Signature	Date

Relationship to Participant

Please note: More information regarding the assistance provided during the consent process should be noted in the medical record for the participant if applicable, noting the role or relationship of the impartial witness.