

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title: Post-Concussion Syndrome in Professional and Amateur Athletes: A Multidisciplinary Study

The Principal Investigator and Project Team: There is a team of research scientists known as the **Project Team** involved in this research and the principal investigator is **Dr. Charles Tator**, neurosurgeon (telephone number 416-603-5889) and the co-investigator is **Dr. Carmela Tartaglia** neurologist (telephone number 416-603-5483)

Funding Source: The study will be financed by the Canadian Concussion Centre, funded through donations made to the Toronto General and Western Hospital Foundation

This Consent Form is addressed to the patient. However, in the case the patient does not have capacity to provide informed consent for themselves the form is given to you as their substitute decision maker for whom informed consent will be obtained for participating in the study.

Introduction:

You are being asked to take part in a research study. Please read this explanation about the study and its risks and benefits before you decide if you would like to take part. You should take as much time as you need to make your decision. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish. Participation in this study is voluntary.

Background and Purpose:

The purpose of this research is to examine the relationship between repeated concussions and late decline of brain function. This problem is suspected to be especially frequent after repeated concussions in sports, but may also occur after concussions in other activities including motor vehicle crashes, industrial injuries or falls.

For this research study, we are asking athletes some of whom suffer from the after-effects of repeated concussions to undergo a series of clinical, imaging and blood tests outlined below in order to examine the effects of repeated concussions on brain function and brain structure. In addition, all participants agreeing to participate in the study will be asked to will their brains to The Krembil Brain Institute Concussion Project at the Toronto Western Hospital with the consent and full knowledge of their families and doctors. However, it is possible to participate in the research without agreeing to a brain donation.

The Project Team is specifically attempting a clinical-MRI-brain tissue research analysis to determine the exact mechanism of the damage to brain tissue following repeated concussions. This condition is known as *chronic traumatic encephalopathy or CTE*, and shows an abnormal protein in the brain called tau-protein, and also shrinkage of the brain. At present, there is no effective treatment for this condition which causes gradual worsening of memory, thinking and movement. In most cases of this condition, the symptoms are similar to Alzheimer's disease but some persons show effects similar to Parkinson's disease. At present, there is no effective treatment for this condition, and therefore, in this study, we are not able to offer any type of neurological rehabilitation program that is known to provide effective treatment. The study will involve 300 athletes and 100 healthy control participants.

The Project Team aims to fully evaluate the relationship between repeated concussions and late deterioration of brain function, and therefore, we will collect information based on the following ten categories:

Procedures:

- 1. Clinical Neurological Examination**
- 2. Magnetic Resonance Imaging (MRI) of the Brain and Spinal Cord**
- 3. Neuropsychological Assessment**
- 4. Behavior Functioning Questionnaires**
- 5. Sampling of Your Blood for Genetic Testing and Other Factors related to Brain Deterioration**
- 6. NeuroTracker**
- 7. Positron Emission Tomography (PET) scan of the brain**
- 8. Eye Scanning**
- 9. Lumbar puncture (LP)**
- 10. Permission to be contacted for follow-up assessments**
- 11. Autopsy and Donation of the Brain and Spinal Cord for Research**

Procedures:

You are being asked to be a participant in this research study because you have had repeated concussions. There is no charge to you for any of the assessments in this study. You are being asked to give your consent separately to each of the ten procedures briefly outlined above. You can choose to participate in all or only some of procedures. You are asked to sign after each section on the line indicated if you wish to participate in that section.

1. Clinical Neurological Examination.

One of the neurologists or neurosurgeons at the Toronto Western Hospital - UHN will conduct a complete neurological examination including taking of the history and performing a physical examination. This examination will take about 1.5 hours and will include complete documentation of your concussions and other history of medical conditions you may have had. You will also be asked to sign consent forms giving your permission to obtain your complete medical history and imaging, and neuropsychological tests from other hospitals, clinics and imaging facilities.

Risks/Discomforts/Inconvenience: There are generally no risks with the clinical assessment.

Consent for the clinical neurological examination: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

2. MRI Imaging of the Brain and Spinal Cord.

Magnetic resonance imaging (MRI) is used to take a picture of your brain and spinal cord. The MRI machine uses no radiation; it uses magnetic fields and radio waves to take a picture of the brain and spinal cord. The MRI will be conducted at the Toronto Western Hospital - UHN. The combined procedures will take about 2 hours. You will be asked if you could have previously had a metallic foreign body embedded in your eye, and if so, you will be asked for a separate consent to give permission for an X-ray of your eyes. This is a routine precaution and always considered in any person undergoing MRI. You will not be directly provided with any MRI test results and a neuroradiologist will not look at the scan. If a researcher has a concern about the scan he/she will forward it to the neuroradiologist on our study, Dr. David Mikulis. In the unlikely event that there are MRI findings of clinical importance, Dr. Mikulis will generate a report that will go to your family physician with your permission.

Risks/Discomforts/Inconvenience: MRI brain imaging is considered to be safe, however, the following risks must be considered. Metal objects in or on your body can move or cause heating. The MRI technologist will discuss this topic with you to determine if you have either foreign metallic objects like shrapnel, or metallic medical implants before determining if it is safe to have the MRI scan.

Having an MRI may cause some discomfort, such as feeling claustrophobic or bored. There is also a loud banging noise during the study, which may be bothersome. You will be given disposable ear plugs. If you are too uncomfortable and prefer not to continue for any reason, you will be removed from the magnet.

Consent for the MRI Imaging: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

3. Neuropsychological Assessment.

You will receive an assessment of your "cognitive" functioning (e.g. attention, memory, problem solving, and mood). You will be asked to carry out some cognitive tests (e.g., learning, reading, drawing) and some questionnaires. The tests are mostly paper and pencil and computerized tests. The assessment will take place at Toronto Rehab - UHN and will take about 3-4 hours to complete. If you become tired during the neuropsychological testing session, you can stop and rest. After the assessment is complete, we will invite you to come in (or to speak by telephone) to find out the results of the assessment and may make recommendations to improve your day to day functioning. We will also provide you with a short written report of these results and recommendations.

Risks/Discomforts/Inconvenience: There are generally no risks with the clinical assessments, There is the possibility that some of the testing and questions may be fatiguing, stressful or produce unpleasant feelings, but you will be able to stop or take a break at any time if you feel too uncomfortable.

Consent for the neuropsychological assessment: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

4. Behavior Functioning Questionnaires.

An interview and some questionnaires about you will be completed by the caregiver, a family member or a close friend. These forms will consist of questions about your social behavior and personality. We would like your consent to contact a family member to fill out these questionnaires. If you have questions concerning the behavioral functioning questionnaires, you can call Dr Carmela Tartaglia at 416-603-5483.

Risks/Discomforts/Inconvenience: There is the possibility that some of the questions may be fatiguing, stressful or produce unpleasant feelings, but you will be able to stop or take a break at any time if you feel too uncomfortable.

Consent for the behavior questionnaires: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

5. Sampling of Your Blood for Genetic Testing and Other Factors related to Brain Deterioration.

It is clear that people respond quite differently to similar degrees of head injury. While some of this difference in response may be because of differences in the nature of the head injury, it is very likely that genetic factors play a role. Therefore, a search for genetic risk factors is part of this research. We will search for the genes and other factors that may be involved. There is also increasing evidence that neuroinflammation (swelling of the brain, spinal cord and nerves) happens in concussion and may be important in postconcussive syndrome and chronic traumatic encephalopathy. We will look at levels of certain blood proteins and search for some markers of neurodegeneration and inflammation. The blood test will be conducted at the Toronto Western Hospital - UHN. Eight test tubes of blood will be taken from a vein in your arm.

We will not be recommending the use of the genetic information from this research study to advise you about your personal risk for developing brain deterioration due to concussions. Finally, because research samples are not handled with the same clinical grade quality control measures and because the samples are treated anonymously as a group, your genetic information generated in this research study cannot be used to guide your medical treatment. Therefore, you will not be given your results or any risk gene discovered by the present research.

This will involve insertion of a needle into the vein in my arm. The blood sample will be kept for 25 years.

Risks/Discomforts/Inconvenience: It may cause temporary discomfort or bruising and rarely, infection, at the site from the needle stick.

Consent for the blood draw and genetic test: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

6. NeuroTracker.

You will be asked to follow four balls that blend with another four on a television screen. These balls then move randomly through true 3D space. Each NeuroTracker play session is six seconds and your performance will be monitored and told to you. The speed of the balls changes based on your responses. It takes 30 minutes to complete the assessment.

Risks/Discomforts/Inconvenience: There are generally no risks with the clinical assessments, including the NeuroTracker. There is the possibility that it may be tiring, stressful or produce unpleasant feelings, but you will be able to stop or take a break at any time if you feel too uncomfortable.

Consent for the NeuroTracker assessment: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

7. PET Scan of the Brain.

You will be asked to undergo a Positron Emission Tomography (PET) scan at the Centre for Addiction and Mental Health (CAMH). A PET scan is a technique of capturing pictures of the brain to look if specific proteins are present in your brain and in what amount. This is a research project and as such the results of the study will not be revealed to you. The PET scan is done by injecting a small amount of chemical [18F] T807 (also known as [18F] AV-1451) in your arm vein and by taking pictures of your brain using the PET camera. The images will be taken on a PET scanner. The injected chemical will provide a detailed picture of your brain. Before being placed in the scan, a small catheter (flexible tube) will be inserted in your arm for blood draw and chemical injection. You will be placed in the scanner 40 minutes after injection. For each scan, you will lie down for 75 minutes on a scanning table so that your head is facing the PET camera. It is very important for you to stay still during the scan therefore we will use a head holder to decrease head movement. Once you are in the scanner, you will be injected with the chemical. The procedure will take approximately 115 minutes. Please note that [18F] T807 (also known as [18F] AV-1451) is an investigational positron emitting radiopharmaceutical used for research purposes and not yet marketed in Canada.

Risks/Discomforts/Inconvenience: The PET scan requires an injection. You may experience some minor discomfort from the insertion of the IV into your vein. This will be very similar to

having a needle for a routine blood test. You may develop a small bruise, however, significant bleeding is extremely rare. You will receive up to 5millicuries (mCi, unit of radioactivity) of [18F] T807 (also known as [18F] AV-1451). The radiation dose to you during a PET scan is comparable to the estimated amount of radiation received from natural sources during one year(in Ontario 2-3 mSv). The total radiation dose from each scan is about 4.5mSv The potential long-term risk from the radiation dose you will receive is uncertain, but such low dosage has never been related to any definite adverse effects. While the radiation exposure from this PET scan is below the limits set by the PET Centre, please let us know if you have participated in any research nuclear medicine procedures that, including the dose received during participation in this study, will bring the total radiation dose over the currently approved guideline of 20mSv in a 12-month period.

Consent for the PET scan: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

8. Eye scanning.

You will be asked to look at sets of images that are presented on a computer monitor while we assess your eye movements. The speed, accuracy and pattern of eye movements will be evaluated. It takes 30 minutes to complete the assessment.

Risks/Discomforts/Inconvenience: There are generally no risks with the clinical assessments, including the Eye scanning. There is the possibility that it may be fatiguing, stressful or produce unpleasant feelings, but you will be able to stop or take a break at any time if you feel too uncomfortable

Consent for the Eye Scanning assessment: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

9. Lumbar punctures (LP).

You will be asked to undergo a lumbar puncture (LP), sometimes called a “spinal tap”. A lumbar puncture is a procedure in which a small amount of the spinal fluid that surrounds the brain and spinal cord is removed by inserting a needle in the lower back. For this procedure, you will be lie on your side and curl up in a ball, or sit up and bend forward, whichever is easier for you. The lower part of your back will be cleaned with antiseptic. The doctor will inject a local anaesthetic (lidocaine, 1%) into the skin of your lower back. When the area is numb, a very thin needle will be inserted into the lower back, well below the level where the spinal cord ends. About 22 millilitres (1½ tablespoons) of spinal fluid will be removed for analysis and storage. Your body replaces this spinal fluid within 1-2 hours.

This procedure will be done in the morning before breakfast and after an overnight fast during which time you will only be allowed to drink water. After the lumbar puncture is completed, you will remain in the clinic for about 30 minutes. You should not do any strenuous physical activity

for the next 24 hours. This includes lifting, bending, doing housework and gardening, or doing exercise such as jogging or bicycle riding.

Risks/Discomforts/Inconvenience: During the procedure, you may have temporary pain and discomfort in your back (15-25% develop this). Headache may occur in 22% of people who undergo a lumbar puncture. Occasionally, a positional headache (lie down feel good but get headache when sit or stand up) may develop, presumably due to leakage of spinal fluid. If this headache persists it may require additional treatment. Uncommonly a blood patch (injection of some of your blood into the lumbar puncture site to patch the spinal fluid leak) may be required. This relieves the headache immediately.

Although very rare (less than 1%), it is possible that you may have an allergic reaction to the local anaesthetic (lidocaine 1%) used for the lumbar puncture. This would cause swelling and a rash on your skin where the anaesthetic was injected. Please tell us if you have ever had a reaction to local anaesthetic before (such as when you were visiting the dentist). Potential but rare risks of lumbar puncture include infection (1 in 10000), damage to nerves in your back (1 in 100000), bleeding into the spinal fluid space (very, very rare - 0 in those not anticoagulated), and death (very, very rare (less than 0.1%)). The risk of these is very small.

Consent for Lumbar puncture (LP): ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

10. Permission to be contacted for follow-up assessments.

In order to investigate whether the effects of repeated concussions on brain function and brain structure is progressive, we will conduct follow-up assessments (which would include: a neurological examination, MRI of the brain and spinal cord, and a neuropsychological assessment, blood test, Eye scanning Behavior Functioning Questionnaires, Lumbar punctures, and PET (optional)). If you give your permission, you will be contacted one year after your initial assessment, and yearly after that for up to 10 years, to schedule follow-up assessments. The follow-up assessments will take about 9-10 hours to complete.

Consent to be contacted for yearly follow-up assessments: ☐ YES ☐ NO

Consent to PET scan of the Brain: ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

11. Autopsy and Donation of the Brain and Spinal Cord for Research.

You will be asked for your permission to perform an autopsy on you and to give permission for your entire brain and spinal cord to be removed from your body and examined after your death. The brain and spinal cord will be stored indefinitely at the University of Toronto Tanz Centre for Neurodegenerative Disease and at the Toronto Western Hospital for future research in this study. If you choose to give consent for this, your next-of-kin will be asked to provide legal consent for

the autopsy. Autopsy results will be released to your next-of-kin. Consent for autopsy is voluntary, and you may withdraw your consent at any time.

You may leave instructions for your next of kin who survive you, that upon your death, your brain and spinal cord are to be made available for neurological research by **The Krembil Brain Institute- Canadian Concussion Centre Project, Toronto** Western Hospital, University Health Network. It is understood that this would not cause any financial burden to your survivors as the autopsy will be performed at no cost to them. You are asking your physician and/or survivors to contact Dr. Carmela Tartaglia (647-971-2876 ; carmela.tartaglia@uhn.ca) or Dr. Charles Tator (416-603-5889; Charles.tator@uhn.ca) immediately in the event of your death as the research cannot be done successfully if the autopsy is delayed. Your next of kin will also be asked to sign the autopsy consent form of the hospital in which you die or the University Health Network.

Consent for the brain and spinal cord donation after death. ☐ YES ☐ NO

Print Study Participant's Name

Signature

Date

Benefits to Being in the Study:

You may or may not receive any direct benefit from being in this study. Information learned from this study may help other people with your condition in the future.

Withdrawal:

You can withdraw from any or all parts of this study without penalty or compromise in any way.

Voluntary Participation:

Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now, and then change your mind later. You may leave the study at any time without affecting your care. You may refuse to answer any question you do not want to answer, or not answer an interview question by saying "pass". We will give you new information that is learned during the study that might affect your decision to stay in the study.

Confidentiality:

Personal Health Information

If you agree to join this study, the study doctor and his/her study team will look at your personal health information and collect only the information they need for the study. Personal health information is any information that could be used to identify you and includes your:

- name,
- address
- date of birth,
- new or existing medical records, that includes types, dates, and results of medical tests or procedures.

The information that is collected for the study will be kept in a locked and secure area by the study doctor for 25 years. Only the study team or the people or groups listed below will be allowed to look at your records. Your participation in this study also may be recorded in your medical record at this hospital, this is for clinical safety purposes.

Research Information in Shared Clinical Records

If you participate in this study, information about you from this research project may be stored in your hospital file and in the UHN computer system. The UHN shares the patient information stored on its computers with other hospitals and health care providers in Ontario so they can access the information if it is needed for your clinical care. The study team can tell you what information about you will be stored electronically and may be shared outside of the UHN. If you have any concerns about this, or have any questions, please contact the UHN Privacy Office at 416-340-4800, x6937 (or by email at privacy@uhn.ca).

The following people may come to the hospital to look at the study records and at your personal health information to check that the information collected for the study is correct and to make sure the study is following proper laws and guidelines:

- Representatives of the University Health Network (UHN) including the UHN Research Ethics Board
- Representatives of the Centre for Addiction and Mental Health (CAMH) including the UHN Research Ethics Board
- Representatives of Health Canada or other regulatory bodies (groups of people who oversee research studies) outside of Canada, such as the United States Food and Drug Administration.

Study Information that Does not Identify You

Any information about you that is sent out of the hospital will have a code and will not show your name or address, or any information that directly identifies you.

All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law.

You will not be named in any reports, publications, or presentations that may come from this study.

If you decide to leave the study, the information about you that was collected before you left the study will still be used. No new information will be collected without your permission.

Genetic Samples

The samples for genetic analysis will be labeled with your identification number, and they will be kept for 25 years to allow us to do any additional tests based on new scientific information that becomes available within the 25 year timeframe.

If in future you wish to remove samples from the sample database, please inform the study team

and your samples will be destroyed. All information collected about your samples to date will continue to be used.

Participation in research may involve a loss of privacy. However, information about you will be handled as confidentially as possible. A Project Team medical record will be created as a result of your participation in this study. Your consent form and some of your test results will be included in this record. Any information that identifies you personally (e.g. name, address) will be removed before the results of the study are published. The information obtained for this research study will be kept locked in a secure area and will only be made available to the Project Team involved in the study and to your doctor or therapist, if you wish.

All records will be stored in a secured database and information transmitted by electronic mail will be protected by password or encryption. Other Project Team doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

Compensation:

You will receive no compensation for your participation in any parts of this research except for reimbursement of some travel expenses as arranged beforehand for any of the Procedures described above and as prearranged with the Project Manager.

Rights as a Participant:

If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost.

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

Separate Consent Forms:

Your next of kin will be required to sign separate forms for “Consent for Autopsy” and “Consent for use of Tissue, Blood, and Body Fluids Obtained at Autopsy for Future Research”.

Conflict of Interest

The Canadian Concussion Centre, the funding source of this study, will pay the hospital for the costs of doing this study. All of these people have an interest in completing this study. Their interests should not influence your decision to participate in this study. You should not feel pressured to join this study.

Questions About the Study:

If you have any questions, concerns or would like to speak to the study team for any reason, please call: Dr. Charles Tator at 416 603 5889, or Dr. Carmela Tartaglia at 416 603 5483 or the Project Manager, Mozghan Khodadadi at 416 603-5800 ext. 4025. They may direct to other members of the Project Team.

If you have any questions about your rights as a research participant or have concerns about this study, call the Chair of the University Health Network Research Ethics Board (REB) or the Research Ethics office number at 416-581-7849 or Dr. Robert Levitan , Chair, Research Ethics Board, Centre for Addiction and Mental Health, at 416 535 8501 ext. 34020. The REB is a group of people who oversee the ethical conduct of research studies. These people are not part of the study team. Everything that you discuss will be kept confidential.

Title: Post-Concussion Syndrome in Professional and Amateur Athletes: A Multidisciplinary Study

Consent:

This study has been explained to me and any questions I have had have been answered. I know that I may leave the study at any time. I agree to take part in this study according to my response to each optional procedure mentioned earlier in this form.

Print Study Participant's Name Signature Date

(You will be given a signed copy of this consent form)

Substitute Decision Maker ☐ After considering the wishes, values, and goals of the patient they would permit the study team to perform study procedures and data collection. I can reverse this decision at any time. The study team will review this consent with the patient when their capacity for consent is regained.

Name of Substitute Decision Maker Signature Date

Relationship to Participant

Your signature means that you have explained the study to the participant named above. You have answered all questions.

Print Name of Person Obtaining Consent Signature Date

Was the participant assisted during the consent process? ☐ **YES** ☐ **NO**
If **YES**, 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 Translator Signature Date

Relationship to Participant

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, and has had any questions answered.

Print Name of Witness

Signature

Date

Relationship to Participant