Forecasting Impairment and Neurodegenerative Disease risk following Traumatic Brain Injury (FIND-TBI)

Participant Information Sheet

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Human Research Ethics Committee Approval Number: H-2021-120

Location: Session 1: The University of Adelaide North Terrace Campus; Session 2: The Clinical + Research Imaging Centre, SAHMRI

1. Introduction

You are invited to participate in the research project described below. This is because you: (1) have experienced a traumatic brain injury (TBI) at some point in the past OR (2) have Parkinson's disease OR (3) have no history of either TBI or Parkinson's disease and are being asked to serve as a healthy control.

Please read the information contained in this document carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2. What is the purpose of this research?

Traumatic brain injury (TBI) is one of the leading causes of death and disability worldwide. However, it is more than a single, one-off event. Many people who have a TBI may experience long-lasting changes in their everyday function that can last for months, or even years, after the initial injury. TBI may also increase the risk of developing certain neurodegenerative disorders,

such as dementia or Parkinson's disease. Despite this, scientists don't yet understand the factors that predict who is at risk for long-term impairment or neurodegenerative disease development following a TBI. This study seeks to understand whether we can use a combination of behavioural tests, brain scans and markers in the blood/saliva in order to predict this risk. If we can predict who is at risk of experiencing lasting difficulties following TBI, or who might go on to develop Parkinson's disease or other neurodegenerative conditions, we may be able to better tailor care for individuals after receiving an injury. This could lead to a better prognosis for the millions of people affected by a TBI annually.

3. Am I eligible to participate in this study?

There are three groups eligible to participate in this study:

(1) People who have experienced a traumatic brain injury (TBI) or concussion after the age of 6
(2) People who have been diagnosed with idiopathic Parkinson's disease
(3) People who have no history of either TBI or Parkinson's disease.

No matter what group you fall in, you must also meet <u>all</u> the following criteria:

- You must be at least 18 years of age
- You must not be suffering from an uncorrected visual or hearing disorder
- You must be deemed eligible to undergo an MRI scan, based on your completion of a safety checklist. These eligibility criteria include:
    - Not suffering from claustrophobia
    - Not pregnant (or suspecting to be pregnant)
    - Not having a metal implant (though most dental work is OK)

In addition, there are some additional eligibility criteria for each of the specific groups:

TBI group:

- You must have suffered a TBI or a concussion after the age of 6

Parkinson's disease group:

- You must have a diagnosis of idiopathic Parkinson's disease by a registered neurologist
- You must have no previous history of TBI

Healthy control group:

- You must not be suffering from a neurological disorder
- You must have no history of brain injury
- You must not be using medication that affects neurological function (e.g., stimulants, sedatives, antipsychotics)
- You must not be diagnosed with a learning disability

If you do not meet the above criteria, you are unfortunately not eligible to participate in the current study.

4. What does participation in this research involve?

There will be **two testing sessions.** Each session will take place over one day, and there are no follow up requirements. You will be informed of the order of the two testing sessions at the time of booking your appointments. We encourage you to attend the sessions accompanied by a member of your family, or a friend.

Session One:
One of the sessions will take place at the University of Adelaide, North Terrace Campus. This session will involve completing a series of questions and tests.
These questions and tests may include:

1. Questions regarding demographic and health information (age, gender, disease history, education, work and leisure activities)
2. Questions regarding current medications
3. Questions regarding vascular risk factors (high blood pressure, tobacco use, weight, history of diabetes, physical inactivity, poor diet, history of high cholesterol/lipids, food preferences)
4. The Unified Parkinson's Disease Rating Scale
5. Short tests that assess motor function (for example, tremor and muscle rigidity)
6. A short test to assess your ability to recognise different smells
7. A series of questions that will look at your sleep patterns, bodily function (e.g. GI function, urinary tract function, sexual function, etc.)
8. The Montreal Cognitive Assessment
9. Short questionnaires that assess mood and personality (depression, anxiety, stress, impulsivity, schizotypal personality)
10. Short questionnaires that assess your quality of life and ability to complete everyday activities
11. A series of tests that assess your reasoning ability, processing speed, working memory, executive function, and general vocabulary.
12. Tests that assess your ability to learn to select correct actions and inhibit incorrect actions.

It will take 2.5-3h in total to complete this session. As a thank you, you will receive a $50 Coles/Myer gift card.

Session Two:
The other session will take place at the Clinical Research Imaging Centre at the South Australian Health and Medical Research Institute (SAHMRI) on North Terrace. This session will involve a brain scan, a blood draw and collection of a saliva sample.

The brain scan will be conducted using magnetic resonance imaging (MRI), a device that uses strong magnets and radio waves to create pictures of the body. The MRI procedure is essentially the same that would be performed for clinical diagnosis; however, this scan is for research purposes only.

MRI is a safe imaging modality that does not involve ionising radiation, so you can have multiple MRIs without any harm to yourself. It involves lying on your back and being moved into the MRI scanner that makes noises whilst brain images are being acquired. All participants are given hearing protection (ear plugs), as well as a safety buzzer should they wish to stop the scan at any point.

If you decide to volunteer to participate in this study, you will first be asked to complete a screening form to make sure that it is safe for you to undergo MRI. It is very important, so please answer the questions carefully, as your answers will indicate whether you meet the screening requirements.

The protocol involves a series of scans, during which you will be asked to stay as still as possible. You will also be asked to complete up to three cognitive tasks in the scanner, including a working memory test and a learning task. The scanning will take no more than 60 minutes.

Once the MRI scan is finished, you will be asked to provide a saliva sample. In order to do this, you will need to allow saliva to pool in your mouth so that the researcher will use a special absorbent pad to collect the saliva.

Finally, you will be asked to allow a researcher trained in blood draw to collect a sample of your blood. We will use these blood and saliva samples in order to look for the presence of certain markers that are related to inflammation and degeneration in the brain.

It will take 1-1.5h in total to complete this session. As a thank you, you will receive a $25 Coles/Myer gift card.

5. Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form, as well as the Biobank Information Sheet and Consent Form, to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you, your relationship with The University of Adelaide, or your opportunity to take part in other studies.

6. What are the possible benefits of taking part in this study?

The results of this research project will likely not provide you with any direct benefit. However, they may provide valuable information to improve the diagnosis, treatment or care of people with traumatic brain injury and Parkinson's disease in the future. By understanding the factors that predict who is at risk of experiencing lasting difficulties following TBI, or who might go on to develop Parkinson's disease or other neurodegenerative conditions, we may be able to better tailor care for individuals after receiving an injury.

7. What are the possible risks and disadvantages of taking part in this study?

Behavioural testing

You may experience fatigue from participating in the behavioural testing session. If you are feeling tired during the testing session, please let the researcher know that you would like to take a break. Refreshments will be available at the session if you desire.

Furthermore, if you experience motor difficulties, there is a small risk that you could lose your balance and fall when stepping on/off the balance platform. In order to reduce this risk, a researcher will help you to step on/off the platform and will monitor you while on the platform.

Mood questionnaires

You will be asked to complete questionnaires that assess levels of depression, anxiety and stress. The questionnaires are not diagnostic tools and cannot be used to diagnose depression or anxiety. However, you may be contacted (via e-mail and telephone) for follow-up based on your scores. The purpose of this follow-up is to provide you with information about available resources for coping with psychological problems should you need them.

Montreal Cognitive Assessment

We will use the Montreal Cognitive Assessment to screen for possible cognitive impairment. Scores below 26/30 are considered abnormal, and we may contact you if your score is below 26 to inform you of the outcome of the test, as an early diagnosis of cognitive impairment could help planning treatment. Please note that this is not a diagnostic test. Mild cognitive impairment is not dementia, and it does not always lead to dementia. It is defined as a noted problem with cognition or brain processing that is unusual for a person's age or education. Mild cognitive impairment does not usually cause any interference with the person's daily level of activities. Although the cause of the syndrome is not fully known, it is possible that it could be triggered by stress or illness. So someone can score below the cutoff score of 26 on the Montreal Cognitive Assessment because of temporary illness, fatigue, or other reasons. Furthermore, a good number of people who score below the cutoff at some point seem to recover their cognitive function and score in the normal range when retested. For these reasons, this test cannot be used to diagnose an illness such as dementia. Such a diagnosis would require further testing.

MRI

MRI is widely used in clinical medicine and considered a very safe test, but you should be aware there could be uncommon physical or psychological effects.

- Some participants may experience claustrophobia.
- If you have a foreign metal object or medical device that you do not know about or do not tell us about, it may undergo movement or stop working within the magnet.
- Any metal accidently brought into the scanner may become projectile. We will therefore ask you to carefully empty your pockets and remove your shoes before entering the scanner room.
- Contact with the inside of the scanner, wires or loops may cause skin burns.
- Changes in the magnetic fields can cause nerve twitching.
- Some participants may experience heating.
- The scanner makes loud noises.
- There is a risk of discovering an incidental finding of uncertain medical significance that may cause anxiety, further tests and/or require disclosure in insurance applications. The scans are not intended to diagnose clinical problems. However, a radiologist will review the images and we will provide a letter stating clinically significant outcomes if appropriate, for yourself or your doctor if preferred.

During the scan, you will be able to communicate with staff through a microphone system in the scanner and you will also be given a safety buzzer to alert staff. There should not any significant discomfort during this procedure. If you notice any discomfort, you should notify the staff.

Before participating, you must also fill out a volunteer screening form to make sure there are no reasons for you not to undergo an MRI. For example, MRI may not be safe in people with particular metal implants, cochlear implants, surgical clips, mechanical heart valves, nerve stimulators, implanted pumps and pacemakers. Please note, however, that most dental work is safe.

If we identify any known risk to you, you will not participate. Please note that, just because you are not able to undergo an MRI for the purposes of this research study, this does not necessarily mean that you cannot have an MRI in the future if medically required.

Saliva sample:
You may experience a dry mouth after providing the saliva sample. If you notice that your mouth is dry, please ask the researcher to provide you with a glass of water.

Blood draw:
Collection of blood from a vein in the arm (called venepuncture) is a safe and commonly used medical procedure. However, like all medical procedures, it is not without its risk. These risks may include bruising or pain at the site of the venepuncture. Other rarer risks include:

- Infection at the site of venepuncture
- Dizziness or fainting
- Nerve damage, haematoma or arterial puncture
- Exposure to bloodborne pathogens

In order to manage these risks, all blood draw will be conducted by an individual trained in venepuncture and in accordance with current best practice standards, as outlined by the

World Health Organisation. All blood draws will be conducted in using appropriate PPE and sterile equipment. Surfaces will be thoroughly wiped down with an alcohol-based cleaner in between participants, and all consumables will be appropriately disposed of following use.

9. Can I see the results of the research project?

We have developed new cognitive tests to assess cognitive performance more precisely. However, because these tests are novel, they have not been standardised. This means that, although one can compare scores of different individuals, it is difficult to interpret these differences in a meaningful way (for example, a given score on a test does not necessarily indicate cognitive decline). For this reason, we will not give you feedback on your results on the cognitive tests. We can only give you feedback on the Montreal Cognitive Assessment and the mood questionnaires, which are standardised tests.

If you wish, however, to find out the aggregate results of the study as they might appear in professional publications, please feel free to contact the Principal Investigator, A/Prof Lyndsey Collins-Praino (Lyndsey.collins-praino@adelaide.edu.au). You may also wish to follow her laboratory's official Twitter page (@CANDL_neuro) for updates on this and other related research. Please note that publications will not include any information that could be used to identify any individual.

10. What will happen to information about me?

All biological samples and data will be de-identified; a unique ID number will be given to all your samples in place of your name, in order to prevent anyone from identifying you from your samples or data. These ID numbers will not correspond to any names, emails, addresses or phone numbers that may be used to identify you. A document linking your name to your unique ID will be kept by the Principal Investigator, A/Prof Lyndsey Collins-Praino, who will store this securely on a computer at the University of Adelaide. She will be the only one able to access this information. This information will only be accessed in the case that a) we find medically significant information, and b) you have requested that we inform you of said information. In general, your samples and data will not be released for any use without your prior consent, unless required by law or by the ethics committee that approved this project. It may also be used to re-contact you in the future to ask for your participation in a follow up study, if you have consented to be re-contacted for that purpose, or to convey the results of mood questionnaires and the Montreal Cognitive Assessment, as explained in Section 7.

Only average results from all participants will be reported in future publications and presentations. In any publication or presentation, information will be provided in such a way that you cannot be identified, maintaining your confidentiality.

Please note that publication and funding requirements may require submission of data or information to controlled access repositories that meet international security and safety standards for sharing with researchers globally. Any data shared via such repositories will be de-identified, protecting your anonymity.

In accordance with relevant Australian privacy and other relevant laws, you have the right to

request access to your information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

11. Who is organising and funding the research?
This project is funded by the Medical Research Future Fund. It is being conducted by A/Professor Lyndsey Collins-Praino, Dr Irina Baetu, Professor Mark Jenkinson, Dr Stephan Lau, Dr Murthy Mittinty, Dr Frances Corrigan, A/Prof Renée Turner of the University of Adelaide; Dr Adam Wells of the Royal Adelaide Hospital; Angela Walls and Dr Andrew Dwyer of SAHMRI; and Dr Maxime Francois and Dr Wayne Leifert of CSIRO. This large-scale study also involves critical input from several other partners, both nationally and internationally, but these individuals will not have access to the study data itself.

Please note that you will not benefit financially from your involvement in this research project even if, for example, knowledge acquired from analysis of your saliva sample and other information collected from you prove to be of commercial value to the institutions with which the investigators are affiliated.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

12. Who has reviewed this research project?
All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the University of Adelaide.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2018). This statement has been developed to protect the interests of people who agree to participate in human research studies.

13. Who do I contact if I have questions about the project?
If you have any questions regarding this study, please contact the principal investigator, A/Professor Lyndsey Collins-Praino (Lyndsey.collins-praino@adelaide.edu.au; +61 8 8313 5488). She will either answer your question directly or direct your question to the relevant co-investigator.

The study has been approved by the Human Research Ethics Committee at the University of Adelaide (approval number H-2021-120). Please contact the Human Research Ethics Committee's Secretariat on phone +61 8 8313 6028 or by email to hrec@adelaide.edu.au if you wish to speak with an independent person regarding concerns or a complaint, the University's policy on research involving human participants, or your rights as a participant. Any complaint or concern will be treated in confidence and fully investigated. You will be informed of the outcome.

14. If I want to participate, what do I do?

Following your reading of this Participant Information sheet, if you wish to participate, please leave your contact information on our recruitment website (borrowmybrain.org/tbi). If you are eligible for the study, we will send you a link to fill out an online survey, and then we will schedule two appointments. You will be asked to sign the consent form on the day of your first appointment, and fill out the MRI safety screening form on the day of your second appointment.

Yours sincerely,

Assoc Prof Lyndsey Collins-Praino, Adelaide Medical School, University of Adelaide
Dr Irina Baetu, School of Psychology, University of Adelaide
Professor Mark Jenkinson, Australian Institute of Machine Learning, University of Adelaide
Dr Stephan Lau, Australian Institute of Machine Learning, University of Adelaide
Angela Walls, Chief Technologist, Clinical and Research Imaging Centre, SAHMRI
Dr Andrew Dwyer, Clinical Director, Clinical and Research Imaging Centre, SAHMRI
Dr Adam Wells, Royal Adelaide Hospital
Dr Murthy Mittinty, School of Public Health, University of Adelaide
Dr Frances Corrigan, Adelaide Medical School, University of Adelaide
A/Prof Renée Turner, Adelaide Medical School, University of Adelaide
Dr Maxime Francois, CSIRO
Dr Wayne Leifert, CSIRO

Mental Health Resources

We understand that some of the questionnaires included in this study might cause feelings of distress or might remind you of events or circumstances that cause you to feel anxious. Should you need to speak to someone immediately regarding your psychological difficulties, please contact your GP or health professional. There are also a number of services that you can access to help you with any difficulties you might experience.

The Australian Government provides access to information and digital resources, as well as information about other free or low-cost counselling and support services for mental health. Please visit **www.headtohealth.gov.au** for more information. In particular, please take note of the following services:

Mental Health Assessment and Crisis Intervention Service: provides immediate help in regard to a crisis in your health or living circumstances.
13 14 65

Lifeline Australia: a crisis support service that provides short-term support at any time for people who are having difficulty coping or staying safe.
www.lifeline.org.au
13 11 14

Beyond Blue: provides support on a range of mental health issues and is available by phone, online chat or email.
www.beyondblue.org.au
1300 22 4636

Suicide Call-Back Service: anyone considering suicide, living with someone who is considering suicide, or bereaved by suicide, can access the Suicide Call-Back Service.
www.suicidecallbackservice.org.au
1300 659 467

MensLine Australia: a telephone and online counselling service for men.
www.mensline.org.au
1300 78 99 78

Open Arms – Veterans and Families Counselling: provides current serving armed forces personnel, veterans and their families free and confidential counselling, group treatment programs, and community and peer networks.
www.openarms.gov.au
1800 011 046

Kids Helpline: a free, private and confidential phone and online counselling service for young people aged 5 to 25 years old.
www.kidshelpline.com.au

1800 55 1800

eheadspace: free online and telephone support and counselling for young people aged 12 to 25 years old, their families and friends.
headspace.org.au/eheadspace
1800 650 890

Blue Knot Foundation Helpline (formerly Adults Surviving Child Abuse)
The Blue Knot Helpline provides information and short term counselling nationally for adult survivors of childhood trauma.
www.blueknot.org.au
email: helpline@blueknot.org.au
1300 657 380, 7 days a week 9am to 5pm AEST.