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PARTICIPANT INFORMATION STATEMENT AND CONSENT FORM

Therapeutic acute intermittent hypoxia and hypercapnia: developing a novel treatment to restore voluntary function after spinal cord injury (limb muscles)

Professor Jane Butler

What is the research study about?

You are invited to take part in this research study. The study aims to understand how breathing a low oxygen and high carbon dioxide gas mixtures may affect the neural connections between the brain and muscles and the ability to perform motor tasks in people with spinal cord injury. The study's results could have implications for rehabilitation techniques that are used in individuals who have nervous system disorders that affect the strength and coordination of their muscles. You have been invited because you a spinal cord injury and have expressed interest in the project or have previously consented to being contacted regarding future research projects.

Who is conducting this research?

Role	***Name***	***Organisation***
Chief Investigator	Prof Jane Butler	NeuRA and UNSW School of Biomedical Science (SBMS)
Co-Investigator/s	Prof Simon Gandevia Prof Janet Taylor Dr Claire Boswell-Ruys Dr Anna Hudson Dr Euan McCaughey Dr Martin Heroux Dr Elizabeth Bye Dr Harrison Finn Dr Sophie Carter	NeuRA and UNSW SBMS Edith Cowan University NeuRA and UNSW SBMS NeuRA and UNSW SBMS NeuRA and UNSW SBMS NeuRA and UNSW SBMS NeuRA NeuRA NeuRA and UNSW SBMS
Student Investigator/s	Dr Anandit John Mathew Miss Chiettha Prajnadewie	NeuRA and UNSW SBMS NeuRA and UNSW SBMS

Research Funder: This research is being funded by NSW Health and the National Health and Medical Research Council.

Inclusion/Exclusion Criteria

Before you decide to participate in this research study, we need to ensure it is okay for you to take part. We are looking to recruit **EITHER** people with chronic motor incomplete cervical spinal cord injury **OR** healthy adults without spinal cord injury.

To be recruited as a person with a spinal cord injury, you must meet the following criteria:

- Be 18-65 years of age

- Have a chronic incomplete cervical SCI (>1-year American Spinal Injury Association Impairment Scale (AIS A-D)
- Be able to make weak contractions of the hand and/or upper arm.
- Be able to breathe independently (without ventilator assistance)
- Have a lung vital capacity of >1 l and a resting oxygen saturation of >96%.
- ***You do NOT have any of the following:***
    - prone to increased blood pressure due to external stimuli that cannot be modulated (i.e. autonomic dysreflexia), or had autonomic dysreflexia in the last 6 months
    - any other brain or nervous system disorder or surgery or any malignancy (cancer)
    - pregnant or think you might be pregnant
    - have a history of epilepsy
    - have any metal implants in your head or any electronic implants in your head or body
    - have been diagnosed with moderate or severe lung disorder
    - are pregnant
    - have been diagnosed with heart failure or serious cardiovascular disease
    - have had any recent change in medications
    - are not able to give informed consent

To be recruited as a healthy person without a spinal cord injury, you must meet the following criteria:

- Be 18-65 years of age
- ***You do NOT have any of the following:***
    - a spinal cord injury
    - prone to increased blood pressure due to external stimuli that cannot be modulated (i.e autonomic dysreflexia), or had autonomic dysreflexia in the last 6 months
    - any other brain or nervous system disorder or surgery or any malignancy (cancer)
    - pregnant or think you might be pregnant
    - have a history of epilepsy
    - have any metal implants in your head or any electronic implants in your head or body
    - have been diagnosed with moderate or severe lung disorder
    - are pregnant
    - have been diagnosed with heart failure or serious cardiovascular disease
    - have had any recent change in medications
    - are not able to give informed consent

Do I have to take part in this research study?

Participation in this research study is voluntary. If you do not want 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 study at any time. Your decision will not affect your relationship with the University of New South Wales, Neuroscience Research Australia or the Prince of Wales Hospital.

If you decide you want to take part in the research study, you will be asked to:

- Read the Participant Information Statement and Consent Form
- Sign the Participant Information Statement and Consent Form if you decide to participate
- Take a copy of this form with you to keep

What does participation in this research require, and are there any risks involved?

COVID-safe plan: COVID screening will be carried out by phone on the day before your visit as well as on the day of visit to NeuRA. All members of the research team have been trained in safe practices for protection against COVID. Adequate personal protective equipment (PPE) will be used by the research team and will be provided for you. Single use disposable mask and tubing will be used and coupled with single use disposable filters that are certified to filter out bacteria and viruses including the SARS-CoV-2 virus.

On your first visit you will be screened by one of the investigators to assess if you fit into the inclusion criteria for this study.

If you decide to take part in the research study, the research team will ask you to complete two testing sessions at NeuRA. Each session is expected to last about 2-3 hours. Sessions will be at least 1 week apart.

In each session, you will be required to breathe gas mixtures that have either low oxygen mixed with high carbon dioxide or normal oxygen levels. Before, during, and after breathing these gas mixtures, measurements from brain, nerves, and muscles will be acquired. These measurements will be acquired numerous times throughout the experiment, and they are described in more detail on the next page.

Salivary sample using a cheek swab: you will be asked to wipe an oral swab along the inside of your cheek at your first laboratory visit. Your sample will be used for genetic analysis that will be limited to genes thought to influence neuroplasticity. The samples will not be used for purposes other than research. Samples will be stored without individually identifiable labelling and will not be used to generate a cell line for genetic testing. This test is voluntary; if you do not wish to provide a saliva sample for genetic testing, you may still continue in the study.

Breathing gas mixtures. In each testing session, you will be required to wear a breathing mask around your nose and mouth. In one session, you will breathe a gas mixture that has low oxygen and high carbon dioxide levels. You will breathe the gas for up to 90 seconds, followed by a 1-minute period of breathing normal air. This will be repeated 15

times, over the course of about 40 minutes. In another session, you will be asked to breathe normal air for the entire 40 minutes. However, you will not be told which gas mixture you are breathing on the two days. *Risks*: Breathing low oxygen mixed with high carbon dioxide gas mixtures for brief periods is unlikely to cause you harm. Such levels are safe for healthy people who are not exercising and have been used safely for people with cervical spinal cord injury. Your oxygen saturation levels will be monitored continuously. If your levels fall below 75% saturation, you will be switched immediately to breathing normal air. It is possible but not likely that you may feel you are breathing a little more than normal and you might feel light-headed. You may also develop a mild headache or tiredness.

Muscle strength testing. To measure the strength of your muscles, you will be asked to push or pull against a rigid device as hard as you can. *Risks:* If your body is not familiar with making strong efforts with your muscles, the muscle strength testing may cause mild muscle soreness. This soreness may last a couple of days. However, it is not a serious health risk. It is a normal response to exercise that your body may not be accustomed to.

Surface electrodes. We will record the electrical activity of your muscles using pairs of stick-on electrodes; this technique is called electromyography. The stick-on electrodes are placed over the target muscles in the hand and/or arm in standard locations. *Risks*: There is a very small chance that the adhesive used to apply surface electrodes can be an irritant for the skin. We will ask you about allergies prior to their application and you will be offered first aid in the rare case of injury.

Electrical stimulation. To measure the excitability of your nerves, electrical current will be passed through surface electrodes placed on your skin over certain nerves. To measure the excitability of your spinal cord, electrical current will be passed between stick on surface electrodes over the mastoid bones behind each ear. The electrical pulses will be short in duration (a small fraction of a second) and will cause brief muscle twitches of the target muscles. In the case of the electrical stimulation behind the ears, the stimulation can also cause brief contractions of the muscles around the neck and jaw. *Risks:* You may find the electrical pulses to be momentarily painful or discomforting. However, they should cause no long-term effects.

In addition, there is a small risk of experiencing autonomic dysreflexia, a form of hypertension which can be triggered by any kind of stimulation in people with a spinal cord injury. Importantly, you should not participate if you are prone to autonomic dysreflexia. All investigators will be aware of this risk and will be trained how to deal with an autonomic dysreflexia event.

Transcranial magnetic stimulation. To measure the excitability of your brain, a magnetic coil will be held over your head and used to activate the parts of your brain that control the muscles in your arms and legs. When the brief magnetic pulses occur, you will hear an audible click from the stimulator. The muscles in your arms or legs will twitch in response to the magnetic pulses. This is done on purpose. It is how we measure how excitable your brain is. *Risks:* The magnetic pulses may cause the muscles of your

scalp to contract, which may cause a light headache that lasts several hours. However, such headaches are rare. Also, there is an extremely small risk that the magnetic pulses will cause an epileptic fit. However, with single magnetic pulses – the type used in the current project – there has only been one case of an epileptic fit in an otherwise healthy individual with no predisposing factors. To reduce this risk, individuals with a history or family history of epilepsy will be excluded from participating in the current project. Also, those who have had a serious head injury or surgery, those who have implanted devices (e.g., pacemakers), and those who might be pregnant will also be excluded. Trained staff will perform all procedures and a medical doctor will be on hand.

Home sleep analysis and oxygen saturation:
We will give you a little mat device that you can place under your bed and a finger clip pulse oximeter to use for up to 7 days. We will then collect the devices from you and the data will be analyzed to assess if you have any periods during your sleep where your breathing is reduced. Periods of reduced breathing during the night can be normal but could also a sign of a condition called obstructive sleep apnoea.
We will use the data to correlate with the other data that we are collecting.

"If you experience any distress or discomfort during testing or afterwards that may be a result of your participation in the study, you should contact your own GP or specialist to follow up on these symptoms. You should also let us know as soon as reasonably possible. In the event of serious distress or discomfort that you consider to be an emergency you should call 000 for assistance."

Will I be reimbursed for participating in this study?
You will be reimbursed your travel expenses up to $100 each way as well as $20 per hour of your time spent at NeuRA completing the procedures of the study. You will be reimbursed immediately after each testing session.

What are the possible benefits to participation?
There is no direct benefit to you as a participant. However, we will use the information from this study to understand if low oxygen gas mixtures can be used in rehabilitation to improve motor function in individuals who have nervous system disorders that affect the strength and coordination of their muscles.

What will happen to information about me?
By signing this for, you are agreeing that it is okay for the research team to collect information about you and use it for the purposes of the study. We will keep your data for at least 5 years after publication. We will store all information about you at Neuroscience Research Australia. Your information will only be used for the purpose of this research study, unless instructed by you, and it will only be disclosed with your permission. All identifying information will be removed and study numbers and participant codes will be assigned to ensure that your identity is preserved. Only the research team will have access to this information.

The results of this research study will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be published, in a way such that you will not be individually identifiable.

The information you provide is personal information for the purposes of the Privacy and Personal Information Protection Act 1998 (NSW). You have the right of access to personal information held about you by NeuRA, the right to request correction and amendment of it, and the right to make a complaint about a breach of the Information Protection Principles as contained in the PPIP Act. Further information on how the NeuRA protects personal information is available on the NeuRA website (www.neura.edu.au)

How and when will I find out what the results of the research study are?
We will report and publish the results from this study in a variety of ways. However, all information published will be done in a way that will not identify you. If you would like to receive a copy of the results you can let the research team know by including your details in the space provided in the consent form.

What if I want to withdraw from the research study?
If you do consent to participate, you may withdraw at any time. You can do so by completing the 'Withdrawal of Consent Form' which is provided at the end of this document. Alternatively you can ring the research team and tell them you no longer want to participate. Your decision not to participate or to withdraw from the study will not affect your relationship with UNSW Sydney or NeuRA. If you decide to leave the research study, the researchers will not collect additional information from you. Any identifiable information about you will be withdrawn from the research project.

What should I do if I have further questions about my involvement in the research study?

The person you may need to contact will depend on the nature of your query. If you require further information regarding this study or if you have any problems which may be related to your involvement in the study, you can contact the following member/s of the research team:

Research Team Contact Details

Name	Prof Jane Butler	Prof Simon Gandevia	Dr Claire Boswell-Ruys
Position	Senior Principal Research Scientist	Deputy Director at NeuRA	Senior Postdoctoral Fellow
Telephone	9399 1608 0438677267	9399 1616 0405141489	9399 1841 0415992525
Email	j.butler@neura.edu.au	s.gandevia@neura.edu.au	c.boswell-ruys@neura.edu.au

We will telephone you the day after each study session to check that you are OK.

What if I have a complaint or any concerns about the research study?
If you have a complaint regarding any aspect of the study or the way it is being conducted, please contact the UNSW Human Ethics Coordinator:

Complaints Contact

Position	UNSW Human Research Ethics Coordinator
Telephone	+ 61 2 9385 6222
Email	humanethics@unsw.edu.au
HC Reference #	HC200664

Consent Form – Participant providing own consent

Declaration by the participant

- ☐ I understand I am being asked to provide consent to participate in this research study.
- ☐ I have read the Participant Information Sheet or someone has read it to me in a language that I understand.
- ☐ I understand the purposes, study tasks and risks of the research described in the study.
- ☐ I provide my consent for the information collected about me to be used for the purpose of this research study only.
- ☐ I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- ☐ I freely agree to participate in this research study as described and understand that I am free to withdraw at any time during the study and withdrawal will not affect my relationship with any of the named organisations and/or research team members.
- ☐ I would like to receive a copy of the study results via email or post, I have provided my details below and ask that they be used for this purpose only.
- ☐ I consent to being contacted by the HREC approved research staff about potential participation in media events.

Consent to saliva swab for genetic testing
This test is voluntary; if you do not wish to provide a saliva sample for genetic testing, you may still participate in the study. Please check the appropriate box:

- ☐ I consent to have my saliva collected and analysed.
- ☐ I do not consent to have my saliva collected and analysed.

Participation in other future studies

- ☐ We may invite you to participate in other future studies. Please indicate below if you give Neuroscience Research Australia permission to contact you for this purpose.
- ☐ I give my permission for the de-identified data collected in this study to be used for future studies by the investigators.

Name: _____

Address: _____

Email Address: _____

Preferred phone number:_____

Preferred mode of contact: email / phone

☐ I understand that I will be given a signed copy of this document to keep;

Participant Signature

Name of Participant (please print)	
Signature of Research Participant	
Date	

Declaration by Researcher*

☐ I have given a verbal explanation of the research study, its study activities and risks and I believe that the participant has understood that explanation.

Researcher Signature*

Name of Researcher (please print)	
Signature of Researcher	
Date	

+An appropriately qualified member of the research team must provide the explanation of, and information concerning the research study.

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation

I wish to **WITHDRAW** my consent to participate in this research study described above and understand that such withdrawal **WILL NOT** affect my relationship with The University of New South Wales or NeuRA In withdrawing my consent I would like any information which I have provided for the purpose of this research study withdrawn.

Participant Signature

Name of Participant (please print)	
Signature of Research Participant	
Date	

The section for Withdrawal of Participation should be forwarded to:

CI Name:	Prof Jane Butler
Email:	j.butler@neura.edu.au
Phone:	02 9399 1608 0438677267
Postal Address:	NeuRA, Barker St., Randwick NSW 2013

☐ I give my permission for Neuroscience Research Australia to contact me in the future to ask if I would like to participate in future studies.