Correlation Between Structure and Function in the Anterior Cingulate Cortex in People Living with Spinal Cord Injury

Principal Investigator: Prof. Cecilia Moody, Dept of Medicine (Neurology), Faculty of Medicine, UBC

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| **Contact for Principal Investigator**  Address: Room P25, 2221 Wesbrook Mall,  Vancouver, BC, V6T 2B5 | |
| Phone: 604-555-5555 | Fax: 604-555-5556 |
| Email: [Cecilia.moody@ubc.ca](mailto:Cecilia.moody@ubc.ca) |  |
| Date:27 Oct 2022 |  |

UBC Ethics Certificate:

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| UBC Ethical Review # | **H55-5555** |
| Approval Date (dd-mm-yy) | **Pending** |
| Expiry Date (dd-mm-yy) |  |

**Please return Protocol Proposal Form and all attachments to the following address:**

**Karina Antonenko**

Administrator

UBC MRI Research Centre

c/o Quantitative Imaging Research Collective

2215 Wesbrook Mall,

Vancouver, BC V6T 1Z3

[karina.antonenko@ubc.ca](mailto:lindac@physics.ubc.ca)

Phone:604-822-7352

Form Completion Checklist

Please ensure that you have completed all parts of this form and attached the required additional documents as listed below:

**Form Sections**

List of collaborators

Brief study abstract with sufficient information to detail how the requested MRI sequences are believed to address the scientific questions

3 sentence project summary for UBC MRI Research Centre website

Unexpected/Incidental Findings

Checklist of requested MRI sequences

Detailed list of MRI sequences with estimated scan time calculation

Table of participant characteristics

Study timeline information

Funding information

Data analysis and transfer requests

**Additional Documents**

All informed consent/assent forms

Copy of ethics certificate

Optional: additional documents to support the study abstract

Optional: Clinical Trial Site procedure manual/MRI Procedure manual

*Thank you for ensuring all sections are complete, this will help to expedite your study’s approval!*

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| **Collaborators** |

Please list all collaborators and affiliations

**INTERNAL** collaborators: **EXTERNAL** Collaborators:

|  |  |
| --- | --- |
| 1. Prof. Brian S. Smith, Dept of Medicine (Neurology), Faculty of Medicine, UBC | 1. Prof. Patricia Khumalo, SFU |
| 2. Prof. Georgia M. Jones, Dept of Medicine (Neurology), Faculty of Medicine, UBC | 2. Prof. Roger Rivera, SFU |
| 3. Michelle Slackenerny, Dept of Medicine (Neurology), Faculty of Medicine, UBC | 3. |
| 4. | 4. |

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| **Study Timeline** |

Requested Start Date (dd/mm/yy) 01/01/2019

Estimated End Date (dd/mm/yy) 31/12/2019

Cross-Sectional Study  Longitudinal Study

Requested scanner time per MR session: \_\_\_1 hr \_\_\_\_\_\_\_\_\_\_\_\_

**Study Summary for Website**

Please summarize your study in no more than three sentences, including a link to your website (if you wish), for inclusion in our “PROJECTS” page on the UBC MRI Research Centre website:

Chronic neuropathic pain has a major negative impact on quality of life and functional independence, and is refractory to treatment for a large proportion of people with spinal cord injury (SCI). Difficulties related to treatment can, in part, be attributed to a poor understanding of pathophysiology underlying the development of neuropathic pain. The objective of our study is to examine the anatomical, functional, metabolic, and physiological phenotype of damage in the anterior cingulate cortex associated with neuropathic pain after SCI.

**Study Summary**

Please provide a summary of up to two pages in length of the proposed research including the background, specific aims, significance of the project, as well as the Research Plan including a justification for how the requested MRI sequences would address the hypotheses. This abstract should provide enough detail to allow evaluation of scientific merit, feasibility at our facility, and potential safety issues.

If necessary, please attach additional materials to support this proposal.

**(page 1 of 2)**

**Study Title:** Correlation Between Structure and Function in the Anterior Cingulate Cortex in People Living with Spinal Cord Injury

**Principal Investigator:** Prof. Cecilia Moody, Dept of Medicine (Neurology), Faculty of Medicine, UBC

Chronic neuropathic pain has a major negative impact on quality of life and functional independence, and is refractory to treatment for a large proportion of people with spinal cord injury (SCI). Difficulties related to treatment can, in part, be attributed to a poor understanding of pathophysiology underlying the development of neuropathic pain.

A key region of the brain involved in pain perception is the anterior cingulate cortex (ACC). Previous studies have demonstrated increased ACC volumes in chronic back pain patients, however, grey matter volumes alone do not provide information on the underlying pathophysiological processes that may contribute to neuropathic pain. Animal studies of chronic pain have suggested that the ACC may exhibit increased resting state activity as well as increase metabolism due to the increased attention to pain that is conducted to this region.

The objective of our study is to examine the anatomical, functional, metabolic, and physiological phenotype of damage in the ACC associated with neuropathic pain after SCI. The ultimate goal is that a better understanding of pathophysiology of SCI will lead to better and more effective treatments for neuropathic pain in the future.

**Hypothesis:** Distinct anatomical, functional, metabolic, and physiological changes in the ACC, measured using advanced magnetic resonance techniques, will provide new information regarding the phenotypes of neuropathic pain after SCI.

To address this hypothesis, we will employ non-invasive quantifiable magnetic resonance imaging and spectroscopy (MRI and MRS, respectively) in the ACC. Adopted as biomarkers of disease pathology in a variety of other central nervous system conditions (e.g., Multiple Sclerosis), these non-invasive MR techniques provide information regarding changes in anatomy and function. To date, neither has been extensively applied in humans with SCI, and has never been previously used for phenotyping neuropathic pain.

**Abstract**

**(page 2 of 2)**

Specifically, we seek to measure:

* Cortical thickness using high resolution anatomical imaging (T1W, T2W)
* Resting state fMRI as a measure of basal neuronal activity in regions that network with the ACC
* Myelin water imaging to determine whether the myelin in the white matter tracts that connect to the ACC are affected due to SCI
* MR Spectroscopy in the ACC to investigate possible changes in markers of metabolism or glial activation (total creatine, total choline, myo-inositol)

Additionally we will include 3 shell diffusion tensor imaging and susceptibility weighted imaging as exploratory markers for tissue structure changes. In the case of participants who require extra time to get settled in the MRI environment, the DTI can be skipped to save time.

This study will recruit 10 SCI patients with chronic neuropathic pain, 10 SCI patients without neuropathic pain to compare functional, metabolic, and structural differences related to neuropathic pain. We will also recruit 20 age, gender, and education matched healthy controls to provide normative data for these measures in the ACC. Furthermore, all participants will be scanned at baseline, and again after 12 weeks to assess whether these functional, metabolic, and structural measures are stable over time.

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| **Unexpected/Incidental Findings**  This section is required to be completed by all studies |

The Centre does not have a routine screening process in place for unexpected or incidental findings - although it does have a procedure for reporting such findings when identified during standard image quality assessments.

The P.I. is expected to have a **Radiologist Collaborator** for the identification and reporting of such findings when:

\* The brain pathology or population under investigation is likely to have unexpected or incidental findings (for example populations likely to have findings not previously imaged)

\* The brain pathology under investigation may impact the ability to differentiate unexpected or incidental findings from known pathology (for example brain injury or unknown manifestation of pathology).

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| **Radiologist who will review images in the event of an incidental finding:**  If you do not have a radiologist collaborator do you request the Centre’s Radiologist to review images for incidental findings? | UBC MRI Research Centre Radiologist |
| If you checked the above box to request that the Centre’s Radiologist review images for incidental findings, please provide a rationale for choosing not to include a radiologist collaborator: | We are not expecting this subject population to have any clinical brain abnormalities and most subjects will have had previous MRI scans as a part of patient care. |
| **Who will disclose incidental findings to participants:**  Do you request the Centre’s Radiologist disclose incidental findings to participants? | Cecilia Moody  UBC MRI Research Centre Radiologist |

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| **Types of Sequences Requested:** *(please mark all applicable categories)* |

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| --- | --- | --- |
| **Qualitative Anatomical Images** |  | **Functional Imaging** |
| T1W  T2W |  | Resting state, # per session \_\_1\_\_ |
| PDW  FLAIR |  | Task based, # per session \_\_\_\_\_\_ |
| Contrast Enhanced |  | Additional devices: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
|  |  | Single Echo  Multi-Echo |
| **Angiography** |  | **Spectroscopy** |
| IV Contrast Enhanced |  | Single Voxel, # per session \_1\_ , |
| Non-IV Contrast Enhanced |  | location(s):anterior cingulate cortex |
|  |  | MRSI |
| **Perfusion** |  |  |
| Arterial Spin Labeling |  | **Quantitative Relaxation Measurements** |
| IV Contrast Enhanced |  | Inversion or Saturation Recovery T1 |
|  |  | Multi-spin-echo T2 (Myelin Water Imaging) |
| **Diffusion** |  | Multi-gradient-echo T2\* Imaging |
| DWI  DTI |  |  |
|  |  |  |
| **Magnetization Transfer** |  | **Susceptibility Weighted Imaging** |
| **MR Elastography** |  |  |
|  |  |  |
| **Other sequences, please specify:**  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | | |
| **Additional equipment or physiological monitoring? Please specify:**  **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** | | |

**Protocol Details**

Please prepare a detailed description of the MRI protocol including estimated time for each MR sequence and total scan time per session. Please include details if any additional equipment is required, such as response boxes or physiological triggering units. If assistance is needed with this please contact [laura.barlow@ubc.ca](mailto:laura.barlow@ubc.ca)

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| **Scan** | **Time** |
| Survey | 0:30 |
| T1W anatomical scan 0.8mm isotropic resolution | 5:50 |
| T2W anatomical scan 1.0 mm isotropic resolution | 4:30 |
| rsfMRI 2.5mm isotropic resolution with TR=2000ms | 5:12 |
| Quantitative T2 (Myelin Water Imaging) using a 48 echo GRASE with 8 ms echo spacing | 5:11 |
| Single voxel spectroscopy in the anterior cingulate gyrus with voxel size 30 x 20 x 15 mm3 | 8:00 |
| DTI 128 directions, 3 shells, 2mm isotropic resolution | 10:00 |
| Susceptibility weighted imaging | 1:20 |
| **TOTAL** | **40:33** |

We would like the data to be collected with the 32 channel head coil.

We will be booking all participants between 9am and 12pm to control for circadian rhythmical cycles in functional and metabolic states.

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| **Participant Characteristics** |

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Pilot Subjects** | **Controls** | **Patients** |
| **Number** | 3 | 20 | 20 |
| **Time points** | 1 | Baseline  Week 12 | Baseline  Week 12 |
| **Age Range** | 20 – 50 years old | 20 – 70 years old | 20 – 70 years old |
| **Cognitive Deficits**  (Please describe) | None | None expected | May have increased prevalence of anxiety about small spaces |
| **Anticipated Mobility**  (indicate all that apply) | Mobile  Mild Assistance  Walking Support  Wheelchair | Mobile  Mild Assistance  Walking Support  Wheelchair | Mobile  Mild Assistance  Walking Support  Wheelchair |

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| **Data Analysis and Transfer** |

Does your study require data analysis provided by the MRI Centre? Yes

Please detail data analysis needs below:

\_ We would like to fit the single voxel spectroscopy data with LCModel. We would also like to request post-processing of the Quantitative T2 data to produce myelin water fraction maps.

Does your study require data transfer to central reader/uploader? No

Please state company/analysis site or centre:

Does your study require a radiologist report? No

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| **Funding** |

Funding Sources: ­­ ­­CIHR

Invoices paid via:  UBC account OR  external account

Is pilot scanner time required and why? For instance, do you require a dry run to test timing, time to develop an fMRI paradigm, or seed data for a grant application?

\_\_\_\_\_\_\_\_\_ Yes, to practice the single voxel spectroscopy placement, test the overall timing, and assess participant compliance \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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Number of PILOT hours requested (maximum 3 hours):3

Is technical development time requested?For instance, will you require MR sequences which are currently not in use at the Centre? No