Progress Report

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Title of Project: Fluid flow in spinal cord cysts

Summary:
Traumatic spinal cord injury is a devastating condition affecting approximately 600 people each year in Australia and 13,000 in the USA. Of these, up to one third will develop syringomyelia. This condition is characterised by the formation of a fluid-filled cyst, which may lead to pain, paralysis, muscle weakness and wasting, loss of reflexes, and loss of sensitivity to pain and temperature. Additional neurological deficits due to syringomyelia are particularly devastating in spinal cord injury patients, who can be transformed from disabled but independent people into patients requiring assistance with basic daily tasks. If syringomyelia affects the brain stem or respiratory function (breathing) it is life-threatening.

Treatment for post-traumatic syringomyelia usually involves surgery to reduce the pressure the cyst places on the spinal cord, by draining the fluid from the cavity, and removing any obstructions to the normal cerebrospinal fluid flow. Most clinical studies report long-term surgical failure rates of approximately 50%. Syringomyelia occurring as a result of spinal cord injury has proven particularly difficult to treat, because the injured spinal cord is at substantial risk of further mechanical damage with any surgery. Determining the factors responsible for cyst formation and resolution is essential to define surgical goals and for improving treatment. We have shown that cardiac pulsations are important drivers of cerebrospinal fluid flow. Breathing, coughing, and straining also affect cerebrospinal fluid flow surrounding the brain and spinal cord (in the subarachnoid space). The possibility that pressure changes that occur in the chest when we breath might contribute to spinal cord cyst formation has not been studied.

This research project will determine the effect of breathing (respiration) on fluid flow into the spinal cord of control animals and in an animal model of post-traumatic syringomyelia. In addition, we will determine if there are distinct pathways for fluid movement into the cyst using electron microscopy to study the ultrastructure at sub-nanometer resolution. A greater understanding of the specific anatomical pathways may provide precise targets for future treatment strategies.

The first aim of the project investigating the effects of respiration on cerebrospinal fluid flow in post-traumatic syringomyelia is currently underway. The control experiments have been completed and analysed. The experimental (post-traumatic

syringomyelia) animal study is ongoing. This project was to be part of a Master of Research Thesis for a student who was going to commence this project in 2020. Due to COVID-19, the student was given another project. Enrolment of new students has been delayed. Given the labour-intensive nature of this work it is necessary to recruit a student (the part-time research assistant salary requested was not funded) to assist with this project. It is expected that this project will be completed in 2022.

The second aim to determine the anatomical pathways for fluid movement into the spinal cord cyst in an animal model of post-traumatic syringomyelia has been completed. It was decided to expand this project by including additional time-points and additional controls to gain greater insight into fluid movement in this disorder. Instead of the 5 animals with post-traumatic syringomyelia as stated in the grant application we used a total of 16 animals. Eight of these were animals with post-traumatic syringomyelia, studied at either 10 min (n = 4) or 60 min (n = 4) following injection with cerebrospinal fluid tracer. The other 8 animals were controls that had surgery to remove the bone surrounding the spinal cord but did not undergo the additional procedure to produce a spinal cord cyst. All these surgeries have been completed, spinal cords have been imaged and analysed. The data obtained during this study has been prepared as a chapter of a PhD Thesis and will be submitted for publication in the peer reviewed journal 'Fluids and Barriers of the CNS' in the next 1-2 months.