ARE THERE DIFFERENCES IN RESPONSE TO ISCHEMIC INJURY ACROSS THE LONGITUDINAL AXIS OF THE HIPPOCAMPUS?

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INTRODUCTION

- Ischemic strokes occur when a vessel supplying blood to the brain becomes blocked and interferes with the delivery of oxygen and nutrients. Despite being the leading cause of death and the third leading cause of death in Canada, the ability to treat stroke-related brain injury is limited primarily due to incomplete understanding of the underlying mechanisms.
- The risk of stroke doubles every ten years after the age of 55; although the incidence of stroke is 2.6% greater in men, during advanced age (80+ years old) the risk of stroke is higher in women (Scott et al., 2012; Heart and Stroke Foundation, 2015).
- The hippocampus, a structure involved in learning and memory, is highly sensitive to ischemia. Experimental literature suggests differences in response to brain injury exist across the longitudinal axis of the hippocampus (see right). However, differences in susceptibility to stroke-related damage between the two poles of the axis (septal and temporal) are incompletely understood (Rotari et al., 1997).
- As the Canadian population ages, the need for better stroke treatment will only become greater. Our research aims to investigate the fundamental factors that may explain the brain’s response to injury, in order to assist in the development of improved pharmacotherapies.

MATERIALS AND METHODS

- Acute Hypocampal Slices Preparation
- Male and female rats will be anesthetized with CO2, and decapitated. Brains will be rapidly removed (TTC) and placed on rocking (37°C) platform immediately before slicing.
- Slices were 350 μm thick (identical thickness), and 45 °C for 20 minutes to be placed into a separate container of ACSF (sham group).
- Chambers and ischemic control (OGD) groups were incubated at 15 °C.
- TTC METABOLISM AND LDH EFFLUX ARE NEGATIVELY CORRELATED AFTER OXYGEN-GLUCOSE DEPRIVATION

A

B

PRELIMINARY RESULTS

- **15 Minute OGD Challenge Does Not Cause Changes in TTC Metabolism Across the Longitudinal Axis**
  - A 15 minute OGD challenge significantly reduces the level of TTC metabolism in septal (0.059 ± 0.004; t = 3.9; p < 0.025) and temporal (0.046 ± 0.008; t = 4.0; p < 0.012) slices, relative to sham slices (0.108 ± 0.03; t = 0.2; p > 0.05), temporal (0.075 ± 0.01; t = 0.2; p > 0.05), and sham (0.074 ± 0.01; t = 0.2; p > 0.05) controls. TTC metabolism was significantly decreased in both the septal and temporal slices (t = 0.05; p > 0.05) on the 15 minute OGD.
  - 10 Minute OGD Challenge Does Not Cause Changes in TTC Metabolism Across the Longitudinal Axis

A

B

- **10 Minute OGD Challenge Does Not Significantly Reduce the Level of TTC Metabolism**
  - A 10 minute OGD challenge significantly reduces the level of TTC metabolism in both septal (0.06 ± 0.01; t = 1.4; p > 0.05) and temporal (0.07 ± 0.01; t = 0.7; p > 0.05) slices, relative to sham slices (0.10 ± 0.03; t = 0.2; p > 0.05), temporal (0.06 ± 0.01; t = 0.2; p > 0.05), and sham (0.07 ± 0.01; t = 0.2; p > 0.05) controls. TTC metabolism was significantly decreased in both the septal and temporal slices (t = 0.05; p > 0.05) on the 10 minute OGD.

- **TTC METABOLISM IS AN ACCURATE, HIGH-THROUGHPUT MEASURE OF SLICE VIABILITY**

A

B

OBJECTIVES AND RATIONALE

OBJECTIVES
- To apply a model of stroke (oxygen-glucose deprivation; OGD) to hippocampal slices, prepared from male and female rats and to quantify damage using a measure of mitochondrial function (TTC metabolism) and cell membrane integrity (LDH efflux).
- To assess differences in response to OGD-related damage between the septal and temporal poles of the hippocampus.

RATIONALE
- OGD is a well-established model of brain injury that mimics the reduction of oxygen and nutrients to the brain seen with ischemia, and permits the assessment of underlying cell death mechanisms.
- The hippocampus is highly sensitive to stroke-related damage, and evidence suggests differences in response to injury exist across the longitudinal axis.
- Response to ischemic injury between the septal and temporal poles has not been thoroughly investigated.
- Research that contributes to the development of improved stroke treatment is necessary given the aging profile of the Canadian population.