44303 - THE ROLE OF INHALED NITRIC OXIDE IN BRAIN INFLAMMATION

Gilbert Blaise, University Montreal, Montreal, QC, Canada;

Yanqin QI, University Montreal;

Rame Taha, University Montreal;

Walid Elybayed, University Montreal;

Introduction

The contribution of inflammation to the progression of neurodegenerative diseases such as cognitive disorder and Alzheimer's diseases is poorly understood. A systemic inflammatory response associated with cardiac pulmonary bypass (CPB) results in the release of cytokines, such as interleukin-1 (IL-1), IL-6, tumor necrosis factor-alpha (TNF- α), and IL-8, which circulate in the blood and communicate with glia and neurons within the brain. It has been demonstrated that inflammatory cells and activated glial cells produce proinflammatory cytokines in response to Lipopolysaccharide (LPS) challenges. We have shown that inhaled nitric oxide (NO) can decrease pulmonary and systemic inflammation following CPB in pigs. Our aim is to investigate INO can modulate brain inflammation and reduce cognitive disorder evoked by systemic LPS administration in rats with and without anaesthesia.

Methods

Institutional animal care committee approved this study. Rats will be used in this research proposal with well validated neurological and neurocognitive tests. The animals have been divided into 4 groups. a: sham group; b: general anesthesia (GA), c: LPS d: GA plus LPS. In each treatment arm, the rats will receive or not INO at 2 concentrations. Ten rats for each group. All of them will undergo neurological and neurocognitive evaluation as well as Morris water maze test. The brain will be removed after craniotomy and prepared for immunocytochemistry staining and in situ hybridization processing.

Results and discussion: Our major findings include the following: 1. We found a significant change in neurocognitive function in the anaesthesia and LPS group compared to the sham group. 2. There is a higher expression of IL-1, IL-6 and TNF- α ; mRNA in LPS and anaesthetic group compared to the sham group using in situ hybridization. 3. We also found more activated astrocytes and glial cells in the brain of the LPS and anaesthesia group compared to the sham group. 4. The expression of IL-1, IL-6 and TNF- α ; has been reduced after administration of inhaled NO in LPS and anaesthesia group. There are no effects of inhaled NO on the sham group.

Conclusion: The results suggest that brain inflammation may contribute to the pathogenic mechanisms that underlie the clinical expression of neurocognitive disorder.