In the United States there are 638 individuals are hospitalized every day secondary to traumatic brain injury (TBI)-related injuries resulting in 176 daily deaths. Men are disproportionately represented in most studies as trauma is male predominance. This has resulted in a critical unmet research need to determine whether there is a different pathophysiology of injury between men and women. In fact, the CDC has reported that 40% of TBI is sustained by women. Women TBI patients differ in long-term neuropsychiatric sequelae such as anxiety and PTSD than are men. Sex hormones such as estrogen and progesterone play a critical role in protecting glial cells and neurons which subsequently protects the brain from edema, necrosis, apoptosis and inflammation. Sex differences have been largely unexplored in both preclinical and clinical TBI studies remains understudied.

**RESEARCH OBJECTIVES**

Recent work in our laboratory has shown that female TBI mice are disinhibited as compared to male mice suggesting greater anxiety-like deficits after TBI as compared male mice. These data suggest a different pathophysiology of injury in female subjects as compared to male subjects after TBI. Microglia, the resident innate immune cell of the brain, are complicit in this process. To this end we hypothesized that microglia would adopt divergent, sex-dependent TBI-associated transcriptional profiles following acute brain injury.

**METHODS**

Top 10 significant p-values and q-values for GO Biological Processes of Male TBI:

- **A.** Homeostatic (p<2.22e-16) (Psma, Txnrd, Cx3cr1)
- **B.** Cytokine-associated (p<2.22e-16) (Ccl3, Ccl4, Il1a, Il1b, Tnf)
- **C.** Male TBI only (P2ry12, Tmem119, Cx3cr1)
- **D.** Female TBI only (Spint1, Tpt1)

**TOP 10 DIFFERENTIAL EXPRESS GENES**

We observed a difference in transcriptional signatures within the microglia of young-adult male and female mice at baseline, which led to a divergent transcriptional response to TBI:

- The top 10 significant p-values in female TBI included glial cell migration (p>0.00002), cellular response to hypoxia (p=1.3 x10^-9), and cellular response to hypoxia (p<2.22e-16).
- Male TBI included cytokine-mediated pathways (p=3.08 x10^-10), transcription regulation (p=6.01 x10^-10), and cellular response to hypoxia (p<1.3 x10^-9).
- **This supports the need for sex to be evaluated as an independent variable in future clinical trial design.**

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