Introduction: Morphine is one of the most effective analgesics available and our lab has
demonstrated that females require 2-3 times more morphine than males to experience the same
level of analgesia. One of the central loci for pain signaling and opioid action is the midbrain
periaqueductal gray (PAG). It has been well illustrated that morphine binds to neuronal opioid
receptors in the PAG, and more recently it was discovered that opioids like morphine bind to
receptors on glial cells in the same region. Morphine binding results in reactive gliosis, (i.e.,
increased activation of microglia and subsequently astrocytes), and our lab and others have
shown that reactive gliosis opposes morphine analgesia. Here we test the hypothesis that the
sexually dimorphic effects of morphine are due to sex differences in glial activity in the PAG.
Specifically, we hypothesize that females have higher levels of PAG glial cell activity, and that
this opposes morphine analgesia. This study aims to 1) determine baseline levels of PAG
microglia and astrocyte activity 2) Determine PAG microglia and astrocyte activity following
acute administration of morphine at multiple time points.

Method: Male and female rats received a single subcutaneous morphine injection and were
sacrificed 15, 30, 45 or 60 minutes following. Control animals received a saline injection and
tissue was harvested at the same time points. Tissue from the PAG was stained to visualize
microglial and astrocytic cell activity. Glial cell activity of experimental animals was compared
to control animals by measuring the density of staining in regions of the PAG. (IACUC Protocol
#: A11015)

Results: Initial results support our hypothesis of sex differences in glia expression within the
PAG. Specifically, baseline glia activity in the PAG of female brains appears to exceed that of
males, with male activity increasing to resemble that of females 30 minutes following morphine
injection. Full analysis is currently underway.

Conclusion: Should our findings support these aims, it would suggest that inhibition of PAG
glia activation will facilitate morphine analgesia for women, greatly benefiting chronic pain
sufferers.