

TITLE: Does Periaqueductal Gray Glial Cell Activity Put Females at a Disadvantage for Pain Relief?

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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.