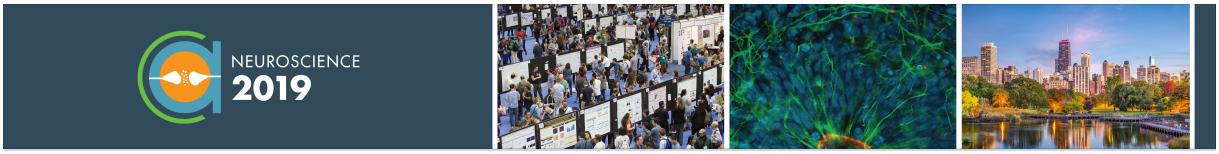

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Session 483 - Pain Models: Pharmacology

Add to Itinerary

483.21 / J42 - Spinal calcitonin gene-related peptide promotes chronic pain plasticity and depolarizes dorsal horn chloride reversal potentials in female but not male mice

October 22, 2019, 8:00 AM - 12:00 PM | Hall A

Presenter at Poster
Tue, Oct. 22, 2019 08:00 AM - 09:00 AM

Session Type
Poster

Grant Support
NIH Grant NS065926

Grant Support
NIH Grant NS102161

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Disclosures
C.A. Paige: None. **I.P. Fernandez:** None. **M. Kumeo:** None. **M. Papalampropoulou-Tsiridou:** None. **L. Lorenzo:** None. **G.L. Mejia:** None. **F.M. Ferrini:** None. **Y. De Koninck:** None. **G. Dussor:** None. **T.J. Price:** None.

Abstract
The majority of patients impacted by chronic pain are women. In our study, we aimed to investigate the potentially sexually dimorphic role of Calcitonin Gene-Related Peptide (CGRP) in three mouse models of chronic pain: hyperalgesic priming, incision, and spared-nerve injury (SNI). Based on emerging findings from the migraine field, we hypothesized that CGRP antagonists would block all three forms of chronic pain specifically in female mice. We induced hyperalgesic priming with an injection of the human IL-6 receptor (IL-6r) or through an incision of the hindpaw. The spared nerve injury was used to induce neuropathic pain. In the hyperalgesic priming experiments CGRP8-37, a CGRP receptor antagonist, was given intrathecally (I.T.) at either the time of IL-6r/incision or PGE2 injection in order to determine if CGRP8-37 could block the establishment of or reverse hyperalgesic priming. For animals with SNI, CGRP8-37 was administered I.T. and PWT was measured following the I.T. injection. In priming induced by IL-6r injection, CGRP8-37 both blocked and reversed hyperalgesic priming specifically in females. In the incision model, CGRP8-37 blocked priming in female mice following PGE2 injection. In the SNI model, there was a transient effect of the CGRP antagonist on mechanical hypersensitivity in female mice only. Our findings demonstrate that blocking CGRP receptors with CGRP8-37 is effective in reducing mechanical hypersensitivity in all 3 models, but only in female mice. Consistent with these findings I.T. CGRP caused a long-lasting mechanical sensitivity specifically in female mice. This CGRP-induced mechanical hypersensitivity was reversed by the KCC2 activator, CLP-257. However, in the IL-6r induced hyperalgesic priming model I.T. CLP-257 reversed hyperalgesic priming in both male and female animals. In spinal dorsal horn electrophysiology experiments CGRP shifted chloride reversal potentials to significantly more positive values but, again, only in female mice. Therefore, CGRP may regulate KCC2 expression and/or activity specifically in females but KCC2 clearly plays a role in promoting

mechanical pain hypersensitivity in both sexes. We conclude that CGRP promotes pain plasticity in female mice, but has a limited impact in male mice, suggesting that CGRP antagonists may be an effective treatment for many forms of chronic pain in females.