**2016 WOMEN’S HEALTH RESEARCH DAY**

**Title of Poster:** Role of Sex Hormones and Sex Chromosomes in Mechanically-Induced Visceral Hyperalgesia in Mice
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**Thematic Poster Category:**  Basic Science Research

**Abstract**

**BACKGROUND:** Characterized by recurrent abdominal pain and altered bowel habits, irritable bowel syndrome (IBS) is more common in women. The mechanisms underlying this sex difference in prevalence remain unclear. The sex-biased proximate factors causing sex differences in phenotype include direct effects of gonadal hormones (organizational or activational) and of genes represented unequally in the genome because of their X- or Y-linkage. To address the role of sex hormones vs. sex chromosomes in the modulation of visceral sensitivity in rodents, we used the “four-core genotypes” (FCG) mice (XX and XY mice with ovaries, and XX and XY mice with testes). **AIM:** To determine the influence of sex hormones and sex chromosomes on the visceral hyperalgesia induced by repeated noxious colorectal distension (CRD) when monitored non-invasively. **METHODS:** Intact and gonadectomized (GDX) FCG male (XY(*Sry*+) and XX(*Sry*+), mice with testes) and female (XX and XY mice with ovaries) (4-6 months old; n=6-8/group) were used. Mice were subjected to 4 sets of isobaric phasic distensions (each set: 3 CRDs at 55 mmHg, 10-s duration, 5-min intervals). Visceromotor response (VMR) was recorded using manometry. The 1st CRD set served as a baseline response. Results were expressed in AUC/min. Data were analyzed using 2-way ANOVA and Bonferroni post-hoc test. **RESULTS:** Visceral hypersensitivity developed in response to repeated noxious CRD in intact XX mice at the 3rd set of CRD, in XY(*Sry*+) at the 4th set, and in XX(*Sry*+) mice in the 2nd, 3rd and 4th sets but not in XY mice. The VMR between groups of males (XY(*Sry*+) and XX(*Sry*+)) and females (XY and XX) was similar. When pooled together, gonadal males exhibited visceral hyperalgesia at the 4th set of CRD (p<0.01) and gonadal females at the 3rd set of CRD (p<0.05), with males presenting higher VMR than females to all sets of CRD reaching significance at the 4th set (p<0.01). Gonadectomy reduced the baseline VMR to the 1st set of CRD in all groups comapred to intact mice. In addition, GDX gonadal males and gonadal females all presented a strong visceral hyperalgesia at the last two sets of CRD, including the 2nd set only for XY female mice. No difference in VMR was detected between groups of GDX males and females. When pooled together, GDX males and females exhibited visceral hyperalgesia at the 2nd, 3rd and 4th set of CRD (p<0.01), and their VMR were comparable. Males GDX exhibited lower VMR at all sets of CRD compared to intact males, unlike GDX females which except for the 1st of CRD, had a similar VMR to CRD than intact females. **CONCLUSIONS:** These data support a major role of sex hormones, but not sex chromosomes, in the modulation of visceral hypersensitivity in response to repeated noxious colorectal distensions under non stress conditions. Supported by NIH DK-57238 (YT), 1K01DK088937 (ML), 1R01NS043196 (AA).