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## Olivia Rau B.A.

Co-author(s): -

Advisor(s): Ellen Casey M.D.

## Differential effects of oral contraceptives on the structure and function of the anterior cruciate ligament

Background: Fluctuations in estrogen and progesterone concentrations affect athletic performance and connective tissue mechanisms during various stages of the menstrual cycle and may contribute to sex differences in sports-related injuries. Prior database studies suggest that oral contraceptives (OCPs) may reduce the risk of anterior cruciate ligament (ACL) injury by 20%. However, the underlying mechanisms for this protective effect are unknown. The estrous cycle seen in rodents is commonly studied to inform understanding of the menstrual cycle. Mouse models assessing OCPs impact on the estrous cycle can inform this clinical phenomenon.

Hypothesis: Mice exposed to OCPs with low ethinyl estradiol and highly androgenic progesterone will demonstrate increased ACL size, stiffness, and load to failure. Hormones were administered in diet, estrous cycle staging was conducted 4x/week. After 8 weeks the mice were sacrificed. Serum hormone levels were measured at time of death and various organs were harvested. Knees were dissected down to the ACL and mechanical testing was performed to calculate force to failure.

Methods: 18 female 12-week old C57BL/6 mice were placed into 3 groups of 6: one group received levonorgestrel (highly androgenic progesterone) and a low dose of ethinyl estradiol (EE), another group received desogestrel (minimally androgenic progesterone) and a high dose of EE, and controls.

Results: The minimally estrogenic and highly androgenic progesterone had a statistically significantly greater load to failure (N) than the highly estrogenic and lowly androgenic and controls.

Significance of Study: Given the high prevalence of OCP use in active females, delineating the musculoskeletal effects of the hormones contained in OCPs is warranted. Findings from this study will add to knowledge of the potential protective mechanisms of OCPs for ACL injury. This data will be used to support further research needed to prevent ACL injuries and personalize care.