

## Can we tackle the adverse health effects of hormonal aging with animal models?

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Ovariectomy (OVX) is a procedure commonly performed on rodents to simulate the effects of menopause in the female body. OVX is done by surgically removing both ovaries, and it enables to study the effects of systemic estrogen deficiency. However, the timing of OVX surgeries is crucial, and variations in this timing may lead to misinterpretation of the results. Common mistakes include performing OVX on animals that are not fully grown or failing to randomize animals into OVX and sham groups based on key outcome variables, such as body mass. When done correctly, OVX replicates the loss of ovarian function in several levels: behavior (decreased physical activity level), body composition (increased adiposity), and metabolic dysfunction (increased insulin resistance). Most excitingly, OVX has shown to replicate the absence of acute response to exercise in circulating extracellular vesicle cargo observed in women. However, OVX does not mimic the menopausal transition experienced by women. With increasing life expectancy, women spend a significant portion of their lives in an estrogen-deficient state. Hence, understanding the mechanisms behind this deficiency is crucial for mitigating potential adverse effects of menopause. In summary, OVX provides valuable insights into the consequences of ovarian hormone withdrawal, but proper timing and randomization need to be considered to draw accurate conclusions. Due to the increase in longevity, addressing menopause-related challenges have become increasingly vital to improve the healthspan of women.