Winter Snow

Developing a Rodent Model of Adverse Menopausal Symptoms

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Menopause is a condition where severe depletion of estrogen levels leads to a cluster of adverse symptoms such as anxiety, cutaneous vasodilation/sudomotor "hot flashes", sleep disturbances, and appetite change (Freeman et al., 2005; Seritan et al., 2010). Previously, estrogen replacement therapy was the first line treatment for menopausal symptoms. However, it is no longer acceptable due to increased risk of cancer (Rossouw et al., 2002). Therefore there is a need for creating non-hormonal therapies to reduce the incidence of adverse menopausal-related symptoms. This is hindered by the limited understanding of menopausal symptoms and a lack of animal models of "hot flashes" (Nelson et al., 2006). Currently, the most accepted model of hot flashes is addicting female rats to morphine then inducing morphine withdrawal using naloxone (a ?-opioid receptor competitive antagonist) to provoke increases in tail temp (an indicator of cutaneous vasodilation). Yet, there is no evidence that the opioid system is disrupted in women with menopause [e.g., naloxone does not provoke "hot flashes" clinically (DeFazio et al., 1984)]. Here we induced a menopausal state by surgically removing the ovaries (OVEX) to deplete estrogen which induces a cluster of adverse menopause-like symptoms that include: 1) increased anxiety; 2) weight gain; and 3) disrupted diurnal skin and core body temperature changes. Additionally, we have developed an alternative model of "hot flashes" where administering yohimbine (an alpha2-adrenergic autoreceptor antagonist that provokes "hot flashes in menopausal women) resulted in "hot flash"-related increases in skin temp in OVEX, but not sham-OVEX, female rats.

References
Seritan AL, Iosif AM, Park JH, Deatherage Hand D, Sweet RL, Gold EB (2010) Self-reported anxiety,