Effect of Experimentally Induced Sleep Fragmentation and Hypoestrogenism on Fasting Nutrient Utilization in Pre-Menopausal Women

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Background: Both sleep disturbance and menopause have independently been associated with weight gain in women. Possible mechanisms contributing to this weight gain may be changes in resting energy expenditure (REE) and/or nutrient utilization. Therefore, in the current study we aimed to examine the effects of experimentally induced sleep fragmentation and pharmacologic estradiol (E2) withdrawal on REE and nutrient utilization in the fasted state.

Design: We studied pre-menopausal women during 5-night inpatient studies repeated in the mid-to-late follicular phase (high-E2; n=21) and following leuprolide-induced hypoestrogenism (low-E2; n=9 completed second visit). During each admission there were two nights of unfragmented sleep [8-h time in bed (TIB)] and three nights of fragmented sleep [9-h TIB]. Sleep was fragmented using an auditory stimulus delivered every 15 minutes that sustained wake for 2 minutes, producing 1 hour of wake after sleep onset. Study diets consisted of 3 meals and a snack each day and were iso-caloric across the two visits. REE and nutrient utilization were assessed in the fasted state via indirect calorimetry and compared between E2 states following unfragmented and fragmented sleep using linear mixed models.

Results: Sleep fragmentation in the high-E2 state increased the respiratory quotient (RQ; +3%; p=0.03) with an accompanying increase in carbohydrate oxidation (+20%; p=0.02) and decrease in fat oxidation (-16%; p=0.03). The same effect was observed in response to E2-withdrawl during unfragmented sleep [increased RQ (+5%; p=0.01) and carbohydrate oxidation (+33%; p=0.01), and decreased fat oxidation (-26%; p=0.01)]. There was no additive effect of sleep fragmentation on nutrient utilization in the low-E2 state suggesting a possible ceiling (RQ and carbohydrate oxidation) and floor (fat oxidation) effect. There was no effect of sleep fragmentation or E2 state on REE.

Conclusion: Both sleep fragmentation and hypoestrogenism were shown to alter fasting nutrient utilization, but not REE, in a manner that may contribute to weight gain in menopausal women. These findings are important for understanding weight gain during menopause, which is characterized by estrogen withdrawal and often accompanied by sleep disturbances.

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