

Behavioral and brain mechanisms underlying sleep disruption-induced obesity**Jennifer A Teske**

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Obesity and inadequate sleep are public health problems that increase risk for chronic disease. Inadequate sleep has emerged as a key contributor to obesity. Thus, obesity interventions aimed at improving sleep in parallel to reducing calorie intake and or increasing energy expenditure (EE) may be more effective at mitigating obesity than interventions that do not address sleep loss. Understanding brain mechanisms that promote positive energy balance through modulation of sleep, energy intake and expenditure may also lead to novel targets for obesity interventions. We developed a rodent model of sleep disruption-induced obesity in male and female rats that is ideal for testing obesity treatments and identifying brain mechanisms underlying sleep disruption induced weight gain. In this model, we show that exposure to pre-recorded environmental noise causes weight gain and hyperphagia in noise-exposed rats relative to rats that slept undisturbed independent of sex and weight gain was exacerbated among rats when sleep disruption was combined with access to

a palatable cafeteria-style diet. Moreover, weight gain in response to sleep disruption alone was paralleled by reductions in physical activity and EE. Next, we investigated whether low brain orexin signaling in the ventrolateral preoptic area (VLPO), a known sleep center in the brain, contributed to weight gain due to inadequate sleep by reducing total EE and physical activity since elevated orexin signaling promotes negative energy balance. In contrast to the response to orexin infusion in the VLPO before sleep disruption, orexin in the VLPO was ineffective after chronic sleep disruption. These data suggest that sleep loss may reduce orexin signaling in the VLPO to in turn stimulate weight gain in response to sleep disruption by reducing physical activity and the rate of energy expended during physical activity. These data have implications for reversing treating individuals who are have obesity and are sleep deprived.

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