Eating a High Fat/High Carbohydrate or Ketogenic Diet Does Not Impact Sensitivity to Morphine-induced Antinociception in Rats with Hindpaw Inflammation

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The obesity epidemic continues to be a pervasive, global concern, and individuals diagnosed with obesity have a higher prevalence of chronic pain. While obesity is thought to be caused by a multitude of factors, one contributing factor that has received attention in recent years is the overconsumption of high fat/high carbohydrate foods. Previous literature has demonstrated that eating high fat/high carbohydrate diets can increase sensitivity of rats to stimulant drugs, such as cocaine, but it is not known if eating a high fat/high carbohydrate diet might impact sensitivity to other drugs, such as opioids (e.g., morphine) in the context of inflammatory pain-relief. Further, not all high fat diets are associated with increased weight gain or obesity. For example, the ketogenic diet (which is high in fat and very low in carbohydrates) has been associated with weight loss. To explore whether these dietary manipulations impact sensitivity of rats to morphine-induced antinociception in a model of inflammatory pain, in the present study 24 female Sprague Dawley rats (n=8/group) ate a standard laboratory chow (17% kcal from fat), a traditional high fat/high carbohydrate chow (60% kcal from fat), or a ketogenic (high fat/low carbohydrate) chow (90.5% kcal from fat). It was hypothesized that rats eating high fat chow would be more sensitive to the effects of morphine than rats eating other diets. Rats ate their assigned diets for 5 weeks before the experimental testing began. Approximately 24-hours before the first test, unilateral hindpaw inflammation was induced by injecting 0.1mL of complete freund's adjuvant (CFA) or saline into the footpad. A saline injection, followed by 4 cumulative injections of morphine (1.0-17.8 mg/kg IP) were administered every 15 minutes, and 13 minutes after each injection, the force that resulted in paw withdrawal was recorded. Morphine tests were repeated once per week, for 4 consecutive weeks. Morphine dose-dependently increased paw withdrawal force across all groups for both the CFA- and saline-injected paws; however, there were no group differences between rats eating different diets during any of the 4 weeks of morphine testing. These results suggest that while dietary factors can impact neurochemistry and sensitivity to other types of drugs, the antinociceptive effects of morphine appear to be comparable regardless of the type of food an individual might consume. Future studies will explore potential sex-differences and assess the impact of dietary manipulation on other opioid-induced effects, including their rewarding and reinforcing effects.

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