Eating a high fat or a ketogenic diet increases sensitivity of rats to the locomotor-stimulating effects of methamphetamine

Ketogenic diets (which are high in fat and low in carbohydrates) have been used for the treatment of epilepsy and have been investigated for weight loss. In contrast, traditional high fat diets (which are not low in carbohydrates) can lead to obesity and weight gain, suggesting these two diets might produce opposing effects. Eating a high fat laboratory chow enhances the sensitivity of rats to the behavioral effects of drugs of abuse (i.e., methamphetamine); however, it is not known if ketogenic chow impacts drug sensitivity. To test the hypothesis that diet would impact sensitivity of rats to methamphetamine-induced locomotion and sensitization, rats eating standard chow (17% kcal from fat, 58% kcal from carbohydrate, 25% kcal from protein), high fat chow (60% kcal from fat, 21% kcal from carbohydrate, 18% kcal from protein), or ketogenic chow (90.5% kcal from fat, 0.3% kcal from carbohydrate, 9.2% kcal from protein) were tested once weekly with cumulative doses of methamphetamine (0.1-3.2 mg/kg; i.p.). Dose-response curves and Area Under the Curve (AUC) were analyzed using two-way repeated measures ANOVAs using Tukey’s multiple post-hoc comparisons tests where appropriate. After 4 weeks, rats eating high fat chow were more sensitive to the locomotor-stimulating effects of methamphetamine at smaller doses (i.e., 0.32, 1.0 mg/kg) than rats eating standard chow. Rats eating ketogenic chow were also more sensitive than rats eating standard chow to the locomotor-stimulating effects of methamphetamine, but only at the largest cumulative dose studied (3.2 mg/kg). These results suggest that traditional high fat diets and ketogenic diets do not always produce identical effects and add to the growing literature demonstrating that diet can impact drug sensitivity. Future research will investigate the impact of these diets on sensitivity of rats to other drugs of abuse.