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### **EATING A HIGH FAT DIET ENHANCES SENSITIVITY OF MALE AND FEMALE RATS TO SEROTONIN SYNDROME**

Drugs that act on serotonin (5-HT) systems are important for the treatment of many conditions, including anxiety, depression, and obesity. However, one adverse effect of these medications is the development of 5-HT syndrome, characterized by tachycardia, mental agitation, and muscle tremors in humans. 5-HT syndrome can be modeled in rats and includes several behaviors, such as lower lip retraction, flat body posture, and forepaw treading. Eating high fat chow increases sensitivity of male rats to lower lip retraction induced by the 5-HT<sub>1A</sub> receptor agonist 8-OH-DPAT; however, it is not known if sensitivity to other 5-HT syndrome behaviors, or behaviors induced by different 5-HT receptor agonists are similarly increased in rats eating high fat chow. To test the hypothesis that eating high fat chow enhances the sensitivity of rats to 5-HT syndrome, male and female rats eating high fat (60% kcal from fat) or standard (17% kcal from fat) chow were tested once weekly with cumulative doses of 8-OH-DPAT (0.01-1.0 mg/kg, s.c.), and two different 5-HT<sub>2C</sub> receptor agonists (lorcaserin [1.0-32.0 mg/kg, i.p.], and WAY 163909 [1.0-32.0 mg/kg, i.p.]). Dose-response curves were analyzed with two-way repeated measures ANOVAs using Bonferroni's multiple comparisons tests where appropriate. After several weeks, rats eating high fat chow were more sensitive than rats eating standard chow to 8-OH-DPAT-induced lower lip retraction and to forepaw treading induced by 8-OH-DPAT, lorcaserin, and WAY 163909. These results suggest that individuals with a history of eating a high fat diet (e.g., patients diagnosed with obesity) might be especially sensitive to the therapeutic and adverse effects of drugs that act on 5-HT receptors. Future considerations are focused on exploring possible sex differences related to these effects.