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INSULIN RESISTANCE ENHANCES THE REINFORCING EFFECTS OF NICOTINE IN FEMALE VERSUS MALE RATS.

Clinical studies have shown that persons with diabetes are more susceptible to the tobacco use; however, it is unclear whether this is due to greater pleasurable effects of nicotine. Our laboratory employs rodent models of diabetes to study the behavioral effects of nicotine. The present study used female and male rodents to examine sex differences in the reinforcing effects of nicotine following a chronic high-fat diet (HFD) regimen that induced insulin resistance. Briefly, adult female and male rats received a HFD regimen for 8 weeks and controls received a regular diet (RD). Separate groups of HFD-treated rats received a low dose of streptozotocin (STZ; 25 mg/kg/sc) in order to facilitate insulin resistance. To determine the magnitude of insulin resistance, all rats first received an insulin injection and glucose levels were assessed 15, 30, 60, 120, and 180 minutes later. The rats were then given extended (23 hour) access to intravenous self-administration (IVSA) of 3 increasing doses of nicotine. Each nicotine dose was delivered for 4 consecutive days with 3 intermittent days of drug abstinence. Our major finding was that the HFD regimen induced insulin resistance, which enhanced the reinforcing effects of nicotine relative to their respective RD controls. With regard to sex differences, the magnitude of this effect was greater in female versus male rats that were insulin resistant. Together, our results suggest that insulin resistance, a hallmark feature of diabetes, enhances the reinforcing effects of nicotine particularly in females. These data imply that greater vulnerability to tobacco use in persons with diabetes is due to enhanced rewarding effects of nicotine.