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Atypical antipsychotic drugs are commonly associated with undesirable side effects including body weight gain (BWG) and metabolic deficits. Many pharmacological interventions have been tested to minimize or prevent these side effects. Preliminary evidence suggested that antidiabetic drugs may be effective in attenuating the BWG induced by antipsychotic drugs. In the first phase, we carried out a 28-day study to standardize the correlated effective dosage of the antidiabetic drug empagliflozin (EMPA) and the antipsychotic drug olanzapine (Ola). Rats were divided into control (vehicle), Ola-4 and Ola-8 (4 and 8 mg/kg/OD, IP, respectively), and EMPA-10 and EMPA-20 (10 and 20 mg/kg/OD, IG, respectively) groups. Both doses of Ola produced a significant increase in the percentage of BWG, however, Ola-4 produced a higher BWG. Also, both the doses of EMPA were able to reverse the effect of Ola-induced BWG; however, EMPA-20 produced a higher reversal in BWG and normalized the rat's body weight. So, we concluded that Ola-4 and EMPA-20 were the most effective dosage for experimental purposes in female Wistar rats. In the second phase of the study, we examined the effect of EMPA-20 on BWG induced by Ola-4 in female as well as male Wistar rats. Rats were divided into six groups based on the dosage they received: group 1 (female control), group 2 (female EMPA-20), group 3 (female Ola-4), group 4 (female Ola-4 + EMPA-20), group 5 (male control), and group 6 (male Ola-4). Ola induced sustained increase in BWG. The subsequent treatment of Group 3 and 4 with EMPA attenuated the Ola-induced BWG in female Wistar rats. In terms of the gender difference, the male control group 5 and male Ola group 6 gained more weight throughout the study as compared to the female control group 1 and female Ola group 3, respectively. However, Ola did not cause any weight difference between male rats treated with Ola in comparison with male control group, thus showing a significant gender difference regarding body weight between male and female Wistar rats regardless of Ola administration. In addition, the present findings showed that EMPA effectively attenuated the Ola-induced BWG in female Wistar rats. These novel findings should help to better understand the underlying molecular and behavioral mechanisms contributing to the observed increase in body weight after treatment.