

Background

High caloric diet (HCD) in diet-induced obesity can be caused by central mechanisms regulating reward-seeking behavior. Dopamine as a neurotransmitter that regulates food intake [1] by the mesolimbic brain circuitry stimulation [2]. Medications that block dopamine D2 receptors increase appetite and result in significant weight gain [3]. Those ones that increase brain dopamine concentration are anorexigenic [4]. However, the role of dopamine in pathological consumption and obesity is not clearly understood.

Dopaminergic neurons in the ventral basal ganglia plays an integral role in the response to salient rewarding stimuli such as drugs of abuse, sex, social bonding, and food [5]. Some current studies in animal models indicate that leptin modulates central dopamine function [6].

Objectives

We supposed that D2 dopamine receptor agonists may influence weight gain and leptin level in genetically unmodified rats with diet-induced obesity due to high caloric intake.

Methods

Male rats ($n=64$, 183.0 ± 14.0 g) were divided into HCD ($n=32$) and standard caloric diet (SCD) groups ($n=32$). HCD and SCD rats had daily intraperitoneal injections of Bromocriptin (1 mg/kg), Rotenone (0.3 mg/kg), dimethyl sulfoxide (DMSO – vehicle, 1 ml/kg) ($n=8$, respectively) during 3 months. Eight rats from both groups weren't injected. Length, weight and caloric intake were recorded twice a week. Leptin levels (immunoenzyme analysis), leptin/weight ratio and rodents' speed, distance, open and closed arms visits and time were discovered by plus maze test at the 1st and 3rd months. Experimental results were compared in subgroups, depends on pharmacological agent with noninjected animals (comparison groups). Nonparametric analysis was performed (SPSS 16.0, $p < 0.05$).

Results

HCD rats showed similar weight gain in the 1st and the 3rd months compared to SCD rodents irrespective to injected agent ($p < 0.05$) (fig. 1).

Weight gain was similar in HCD group with lowest weight gain in HCD rats received Rotenone ($p > 0.05$) (fig. 2).

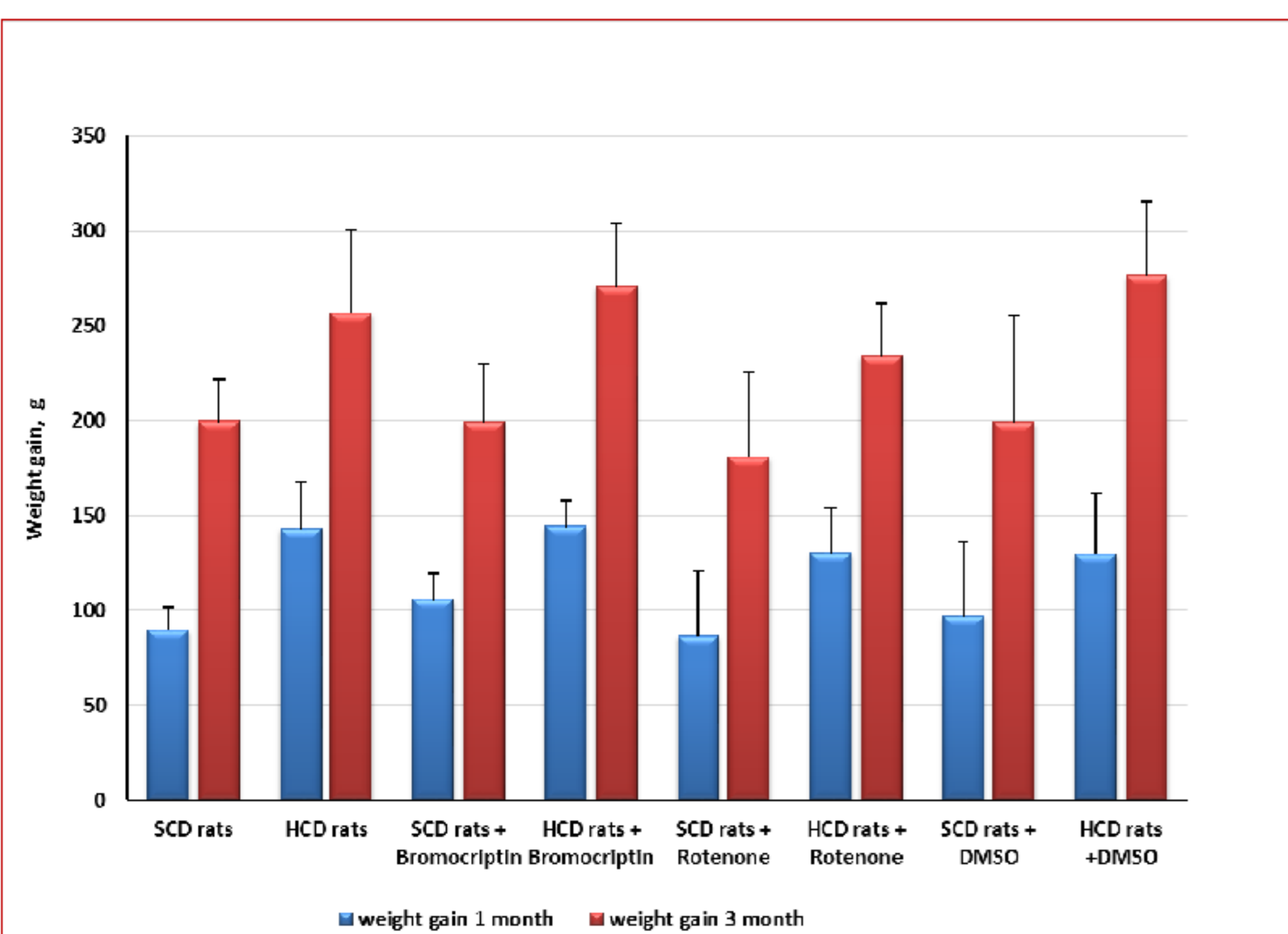


Figure 1. Weight gain in the 1st and the 3rd months depends on the injected agent and caloric intake

Results

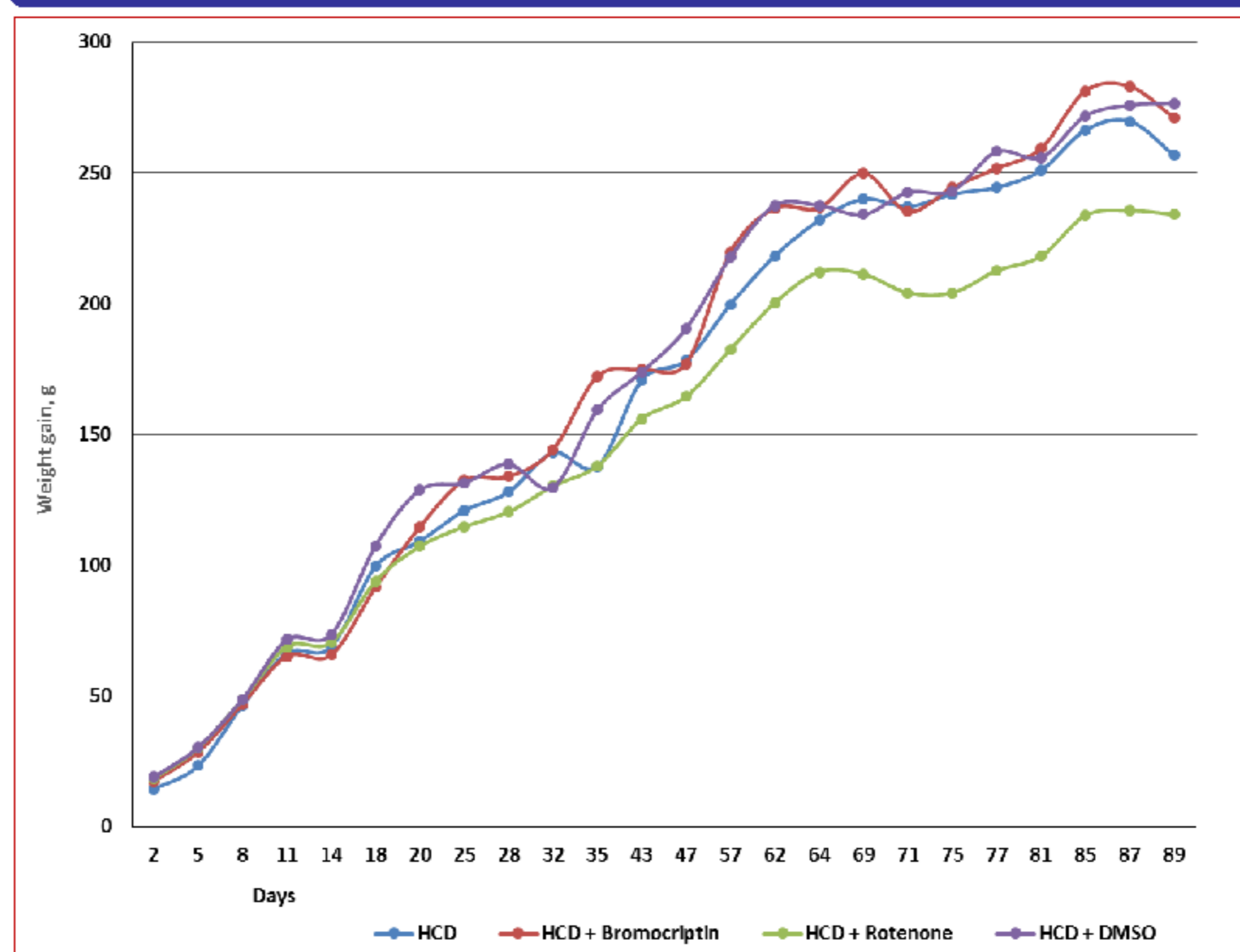


Figure 2. Three-month weight gain in HCD rats depends on the type of injected agent ($p > 0.05$).

Speed and distance had no changes in HCD group after 1 month (fig. 3) but open arm visits significantly decreased in HCD rats injected with Bromocriptin® ($p < 0.05$) (fig. 4).

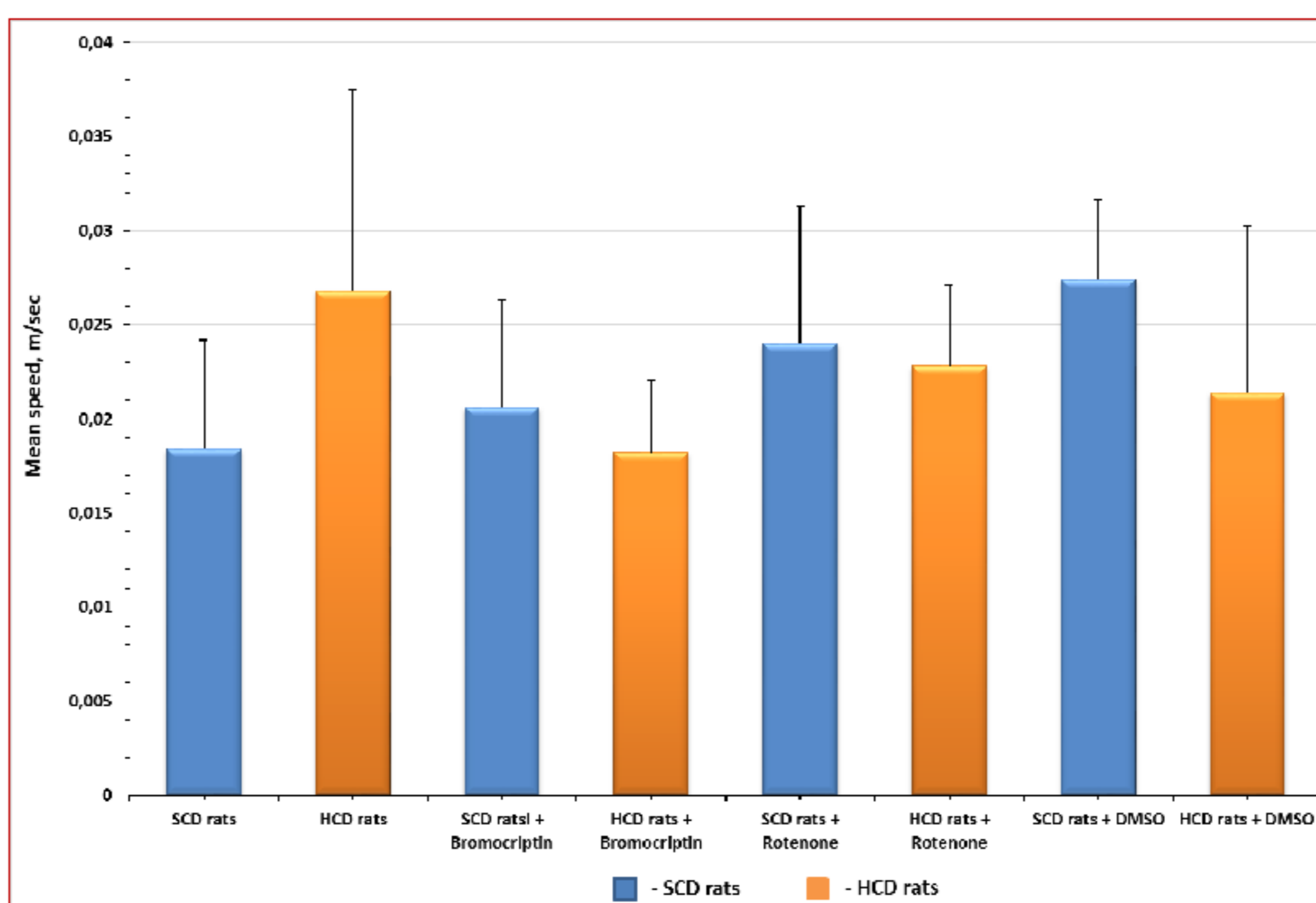


Figure 3. Mean speed in 1 and 3 months in all groups of rodents depends on the type of injected agent

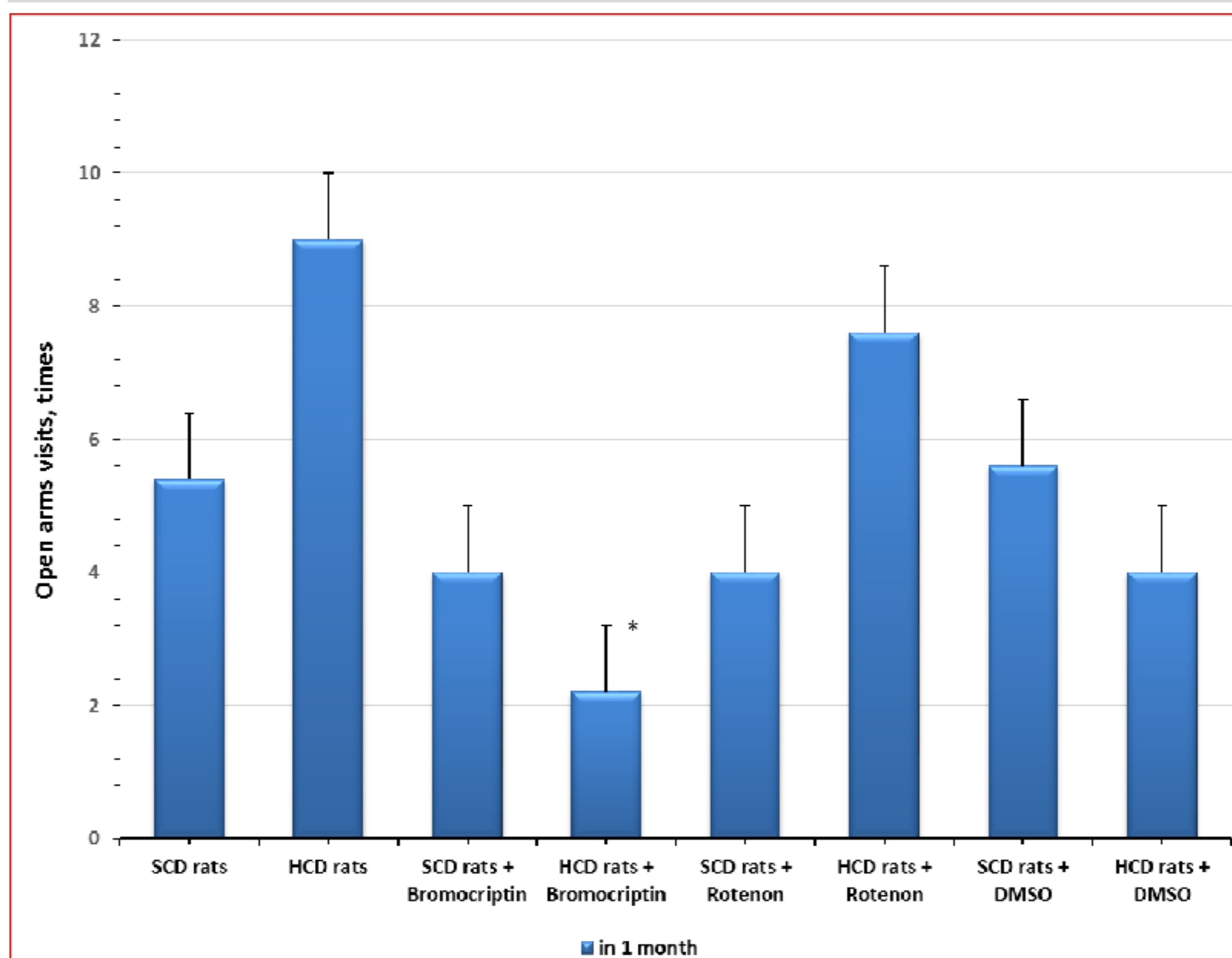


Figure 4. Open arms visits in 1 months in all groups of rodents depends on the injected agent, * - $p < 0.05$

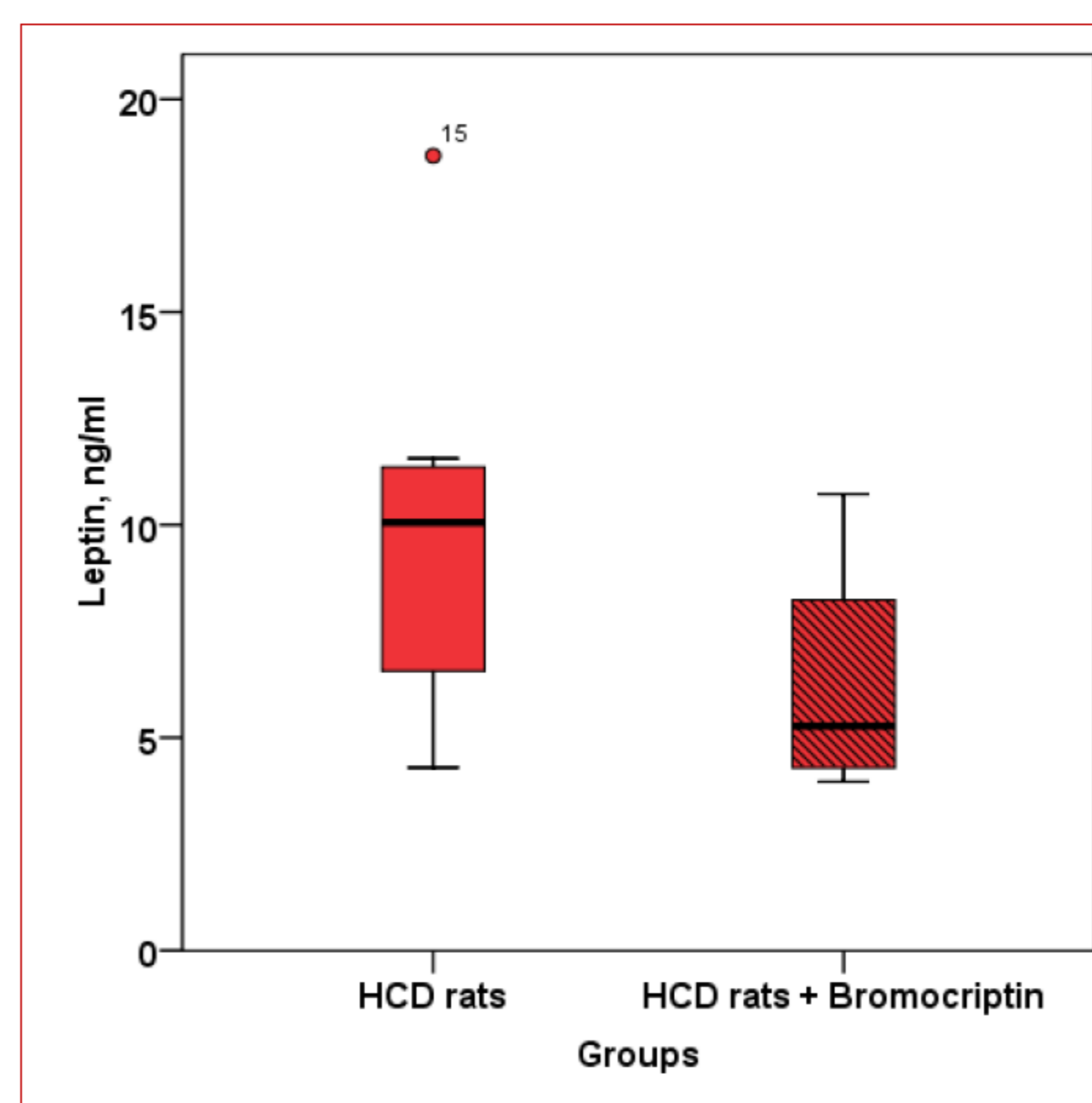


Figure 5. Leptin levels in high caloric diet rats with or without Bromocriptin after three month injections.

Results

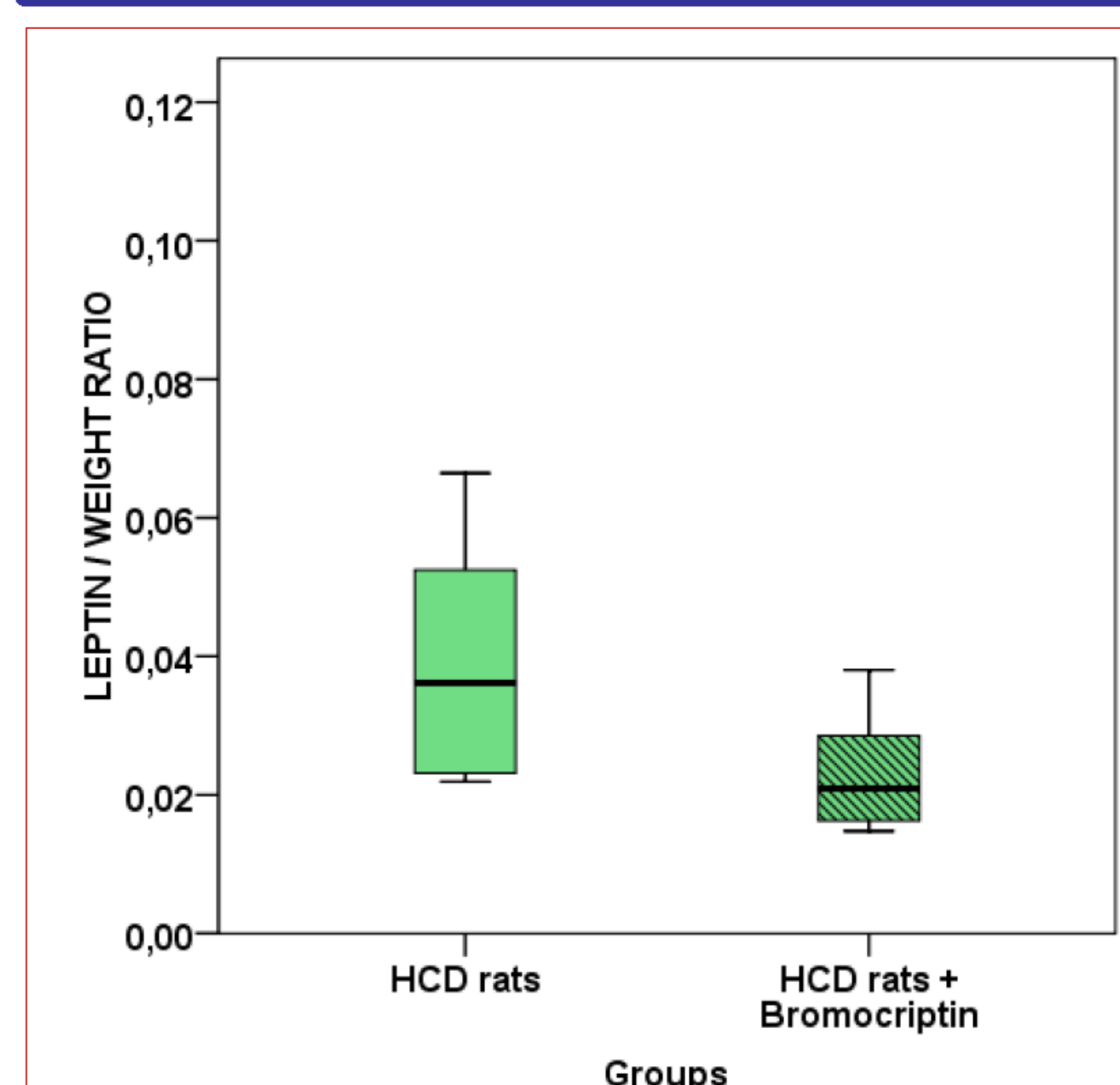


Figure 6. Leptin / Weight ratio in high caloric diet rats with or without Bromocriptin after three month injections.

Leptin (fig. 5) and leptin/ weight ratio (fig. 6) decreased after 3 months of Bromocriptin injections in HCD rats ($p = 0.05$ and 0.005 comparatively).

Leptin (fig. 7a) and leptin/ weight ratio (fig. 7b) levels were extensively lower in Bromocriptin injected HCD rats in 3 month concerning to the 1st one ($p < 0.05$).

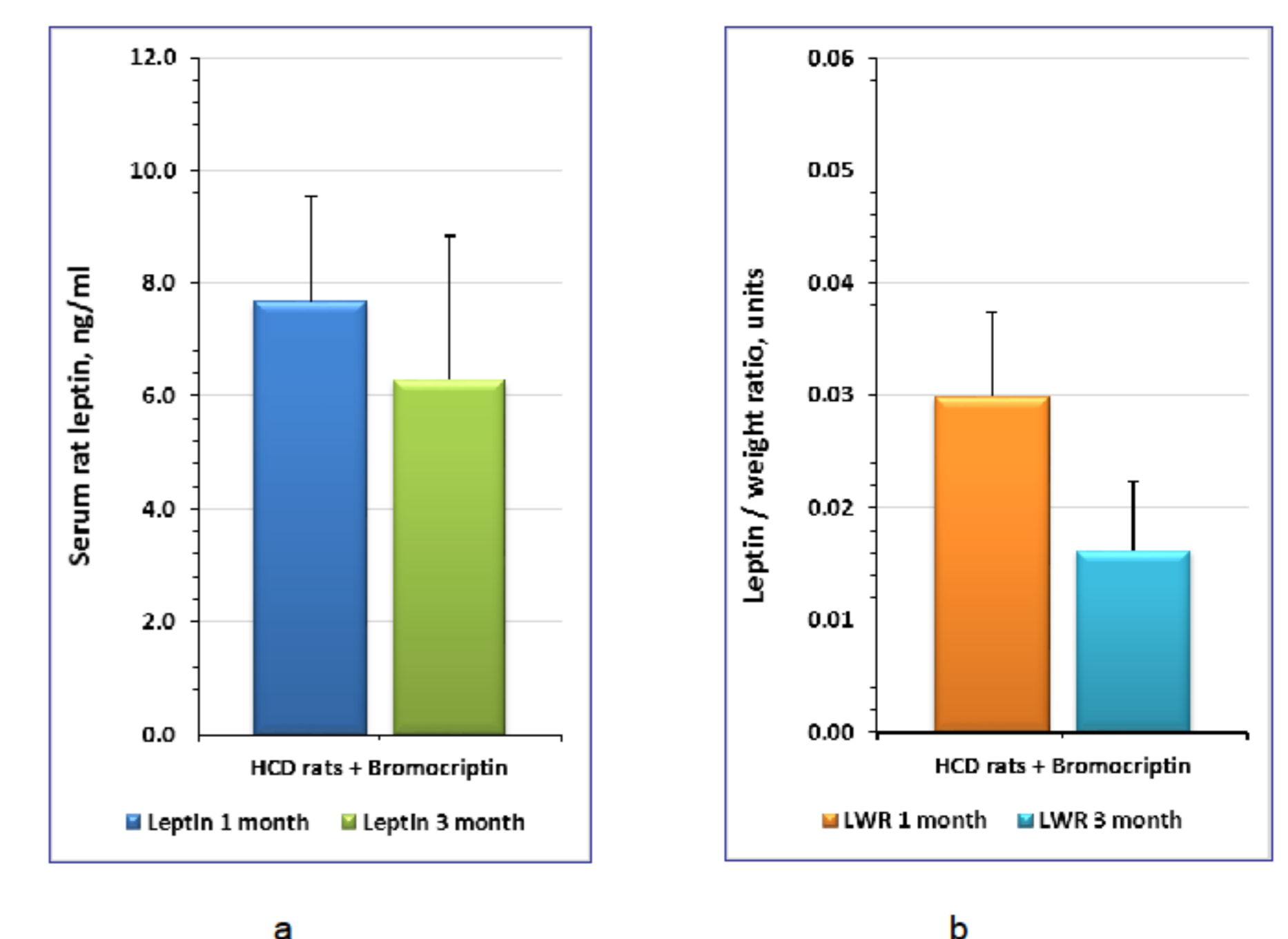


Figure 7. Serum leptin (a) ($p = 0.05$) and Leptin / Weight ratio (b) ($p = 0.021$) levels in Bromocriptin injected HCD rats in 1 and 3 month of experiment.

Conclusions

In rats with high caloric intake, long-term Bromocriptin injections prevent leptin resistance. Neurotoxic Rotenone effect leads to weight gain diminishing in rats with diet-induced obesity.

References

- Balcioglu A., Wurtman R.J. Effects of phentermine on striatal dopamine and serotonin release in conscious rats: in vivo microdialysis study. *Int J Obes Relat Metab Disord.* 1998; 22: 325–28.
- Martel P., Fantino M. Mesolimbic dopaminergic system activity as a function of food reward: a microdialysis study. *Pharmacol Biochem Behav.* 1996; 53: 221–26.
- Baptista T. Body weight gain induced by antipsychotic drugs: mechanisms and management. *Acta Psychiatr Scand.* 1999; 100: 3–16.
- Wang G-J., Wolkow N.D., Wong C.T., et al. Behavior and cardiovascular effects of intravenous methylphenidate in normal subjects and cocaine abusers. *Euro Addict Res.* 1997; 3: 49–54.
- Berridge K.C., Robinson T.E. What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? *Brain Res Brain Res Rev.* 1998; 28:309–369.
- Leininger G.M., Jo Y.H., Leshan R.L., et al. Leptin acts via leptin receptor-expressing lateral hypothalamic neurons to modulate the mesolimbic dopamine system and suppress feeding. *Cell Metab.* 2009; 10:89–98.

Disclosure

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