EFFECTS OF NEUROPEPTIDES IN SPONTANEOUSLY HYPERTENSIVE RATS

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Introduction

Spontaneously hypertensive rats (SHR) have lower calorie intake and body weight (BW) than that of age-matched controls (Fig. 1). Their BW does not reach that of controls even on a high-fat diet. We assumed a dysregulation of energy homeostasis, an enhanced efficacy of anorexigenic (reduction of food intake [FI]) and diminished effects of orexigenic (induction of FI) regulatory peptides in the background.

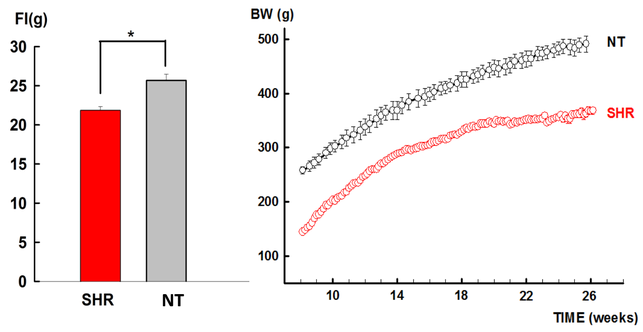

Fig. 1: Daily food intake (FI) and body weight (BW) of SHR and NT rats.

Aims

We aimed to study FI-associated effects of major orexigenic (neuropeptide Y [**NPY**]) and anorexigenic (alpha-melanocyte-stimulating hormone [**alpha-MSH**], cholecystokinin [**CCK**]) peptides and those of a selective melanocortin antagonist (**HS024**) in SHR rats.

Methods

Food intake of 3- and 6-month-old male SHR rats and normotensive Wistar rats (NT) was recorded in an automated FeedScale system upon an intracerebroventricular (ICV) alpha-MSH-injection (5 µg, spontaneous night-time FI), during an ICV HS024-infusion (1 µg/h 7 days), upon an ICV NPY-injection (5 µg, induced day-time FI) and upon an intraperitoneal (IP) CCK-injection (5 µg, day-time re-feeding following 48-hour fasting). The control groups received pyrogen-free saline (PFS). BW was measured daily manually. For the statistical analysis ANOVA tests were used.

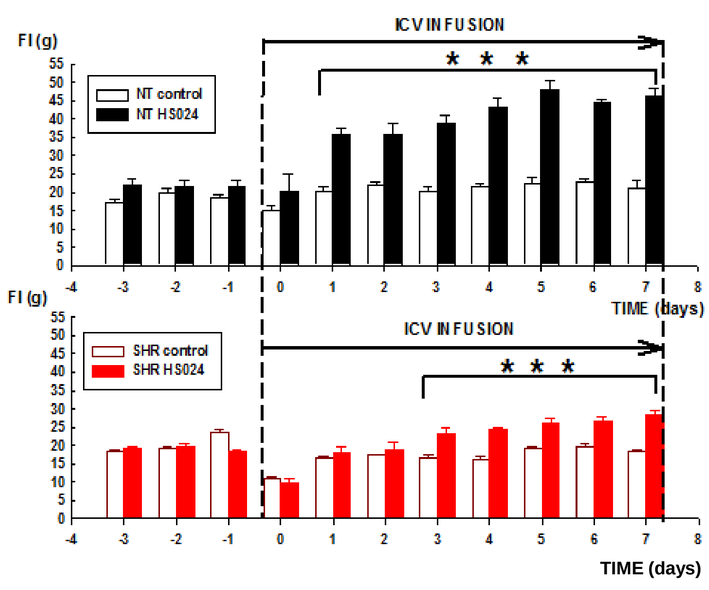

Fig. 2: Effect of ICV HS024-infusion on FI during 7 days in SHR and in NT rats.

Results

1) The melanocortin antagonist HS024 started to increase FI and BW in the NT group from the first day, in SHR animals only from the third. (Figs. 2, 3)

2) The alpha-MSH-injection reduced the FI of SHR rats more efficiently (50% reduction instead of 30%). (Fig. 4)

3) Orexigenic effect of NPY was smaller in SHR rats than in the age- and BW-matched (2-month-old) NT groups. (Fig. 5)

4) FI of SHR was inhibited by CCK more efficiently (47% vs. 34%) than that of the control group. (Fig. 6)

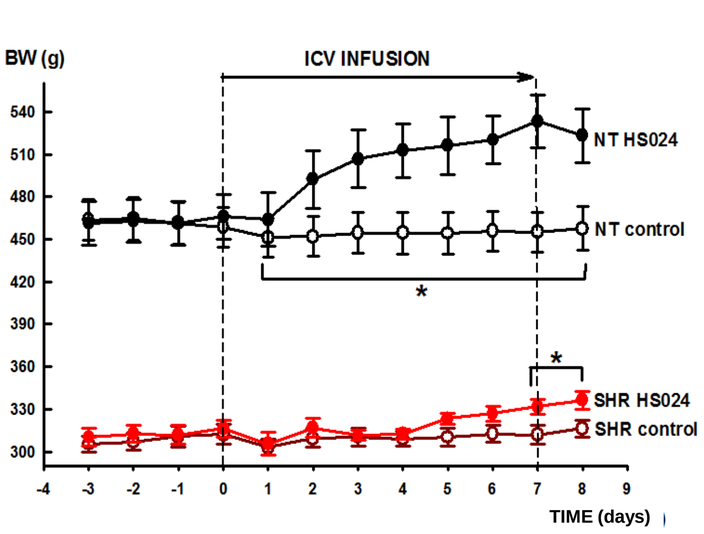

Fig. 3: Effect of ICV HS024-infusion on BW during 7 days in SHR and in NT rats.

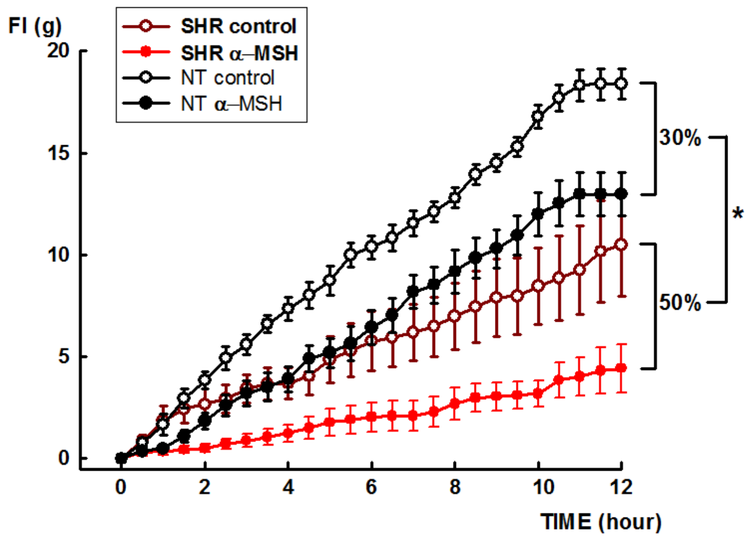

Fig. 4: Effect of ICV alpha-MSH injection on FI in SHR and in NT rats.

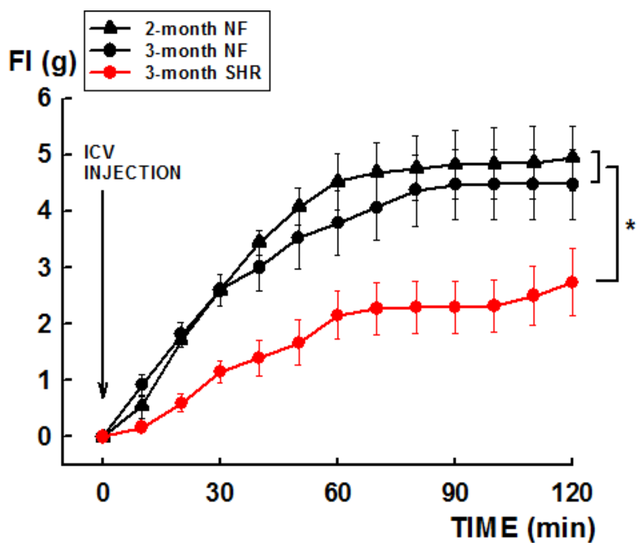

Fig. 5: Effect of ICV NPY injection on FI in SHR and in NT rats of different age-groups.

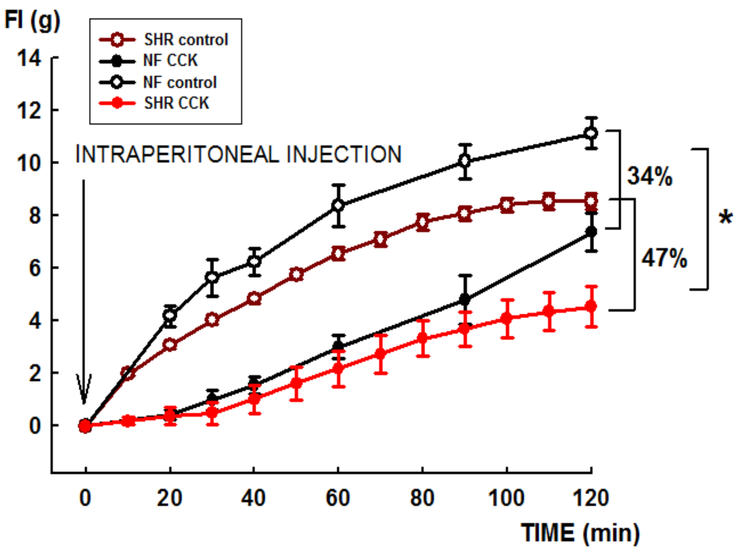

Fig. 6: Effect of IP CCK injection on FI in SHR and in NT rats.

Conclusion

SHR rats showed enhanced responsiveness to the melanocortin and CCK administration, a diminished one to the NPY injection.

In SHR rats, the melanocortin antagonist infusion inhibited endogenous melanocortin-effects only with delay.

According to our results, the regulatory disorder of BW in SHR rats may be explained by **enhanced** efficacy of **anorexigenic peptides** and **diminished** efficacy of **orexigenic** ones.

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