

Towards the roles of Kisspeptins in the Control of Gonadotropic axis: Focus on Peripheral Signaling in Androgen-dependent Tissues in the Experimentally Induced Model Hypogonadotropic Hypogonadism in Male Rats

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Background. Kisspeptins, ligands of G protein-coupled receptor 54 (GPR54) encoded by the KiSS-1 gene, have recently emerged as key gatekeepers of the gonadotropic axis. Unlike its role at the hypothalamus on GnRH secretion, the effects of kisspeptins on gonadal and other peripheral tissues need to be clarified.

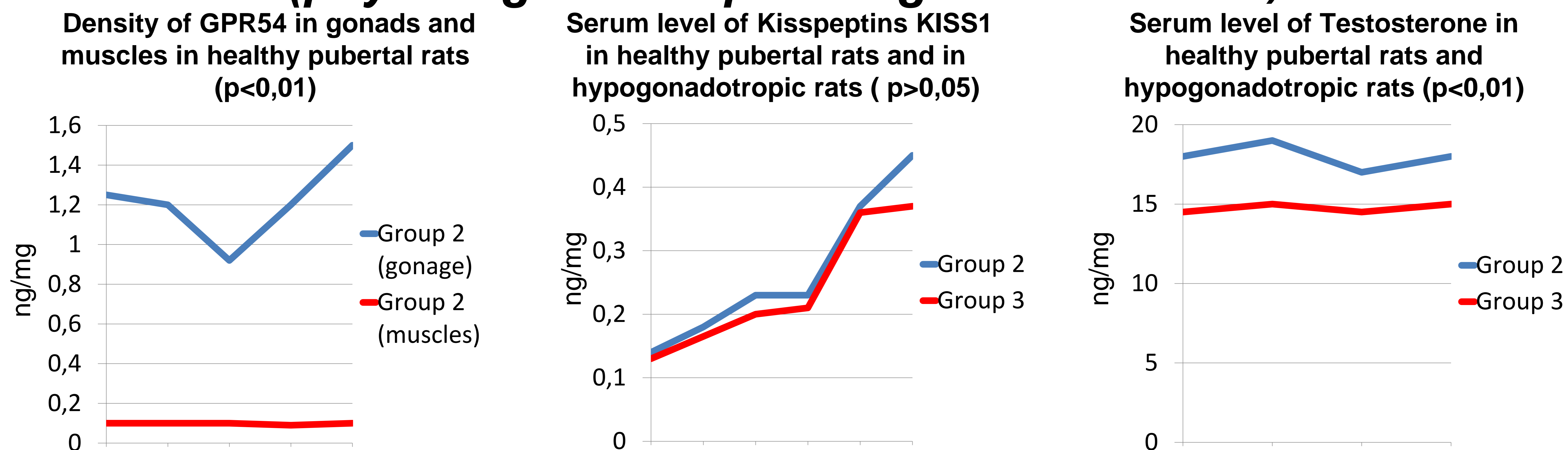
Objective. To investigate the impact of experimentally induced hypogonadism on kisspeptins signaling in androgen-dependent tissues and blood.

Methods. Wistar male rats (29 in total) were used. Rats were divided into four groups. Group 1 (control, prepubertal rats aged 2 months, n=7). Group 2 (control, pubertal rats aged 4 months, n=6). Group 3 (unilaterally gonadectomized (ULG) in neonatal period). Group 4 (ULG treated with testosterone (T) propionate 5 mg/kg/d for 10 days). In all groups the density of GPR54 in testes, muscle as well as serum kisspeptin and T levels were examined. The data was expressed as median values (Me) that were compared by Wilkoxson criterion.

Results. Density of GPR54 in gonads in group 3 was lower than in group 2 (Me 0,88 ng/mg vs 1,13 ng/mg, $p < 0,05$) and similar to group 1 (Me 0,92 ng/mg). Unlike above, density of GPR54 in muscle in groups 1,2,3 there weren't any differences (Me 0,1; 0,12; 0,13 ng/mg, $p > 0,05$). Generally, density of GPR54 in group 2 in gonads was significantly higher than in the same group in muscle (Me 0,784 ng/mg vs 0,114 ng/mg, $p < 0,01$). In the group 3 a significant decrease in serum levels of T (Me 15,39 ng/mg) in comparison with group 2 (Me 20,02 ng/mg, $p < 0,01$) was detected. Serum levels of kisspeptins in both groups were the same (0,27 ng/mg and 0,26 ng/mg, $p > 0,05$). Treatment with testosterone propionate of group 4 rats lead to increase of serum level of T (from 15,39 ng/mg to 26,26 ng/mg, $p < 0,01$), but didn't modify the density of GPR54 in gonads (Me 0,79 ng/mg).

Conclusions. Hypogonadism lead to decrease of kisspeptins signaling in peripheral androgen-dependent tissues. Serum level of kisspeptins is physiologically low and it probably can't be used as a marker of kisspeptin system activity. Testosterone treatment is not effective enough; new therapeutic methods are required.

Kisspeptins Peripheral Signaling in Androgen-dependent Tissues (physiological and pathological conditions)



Influence of treatment with testosterone on KISS/KISS1R (testosterone propionate 5 mg/kg/d for 10 days)

