

Replacement of the neonatal leptin surge during maternal deprivation normalizes some endocrine parameters but exacerbates others

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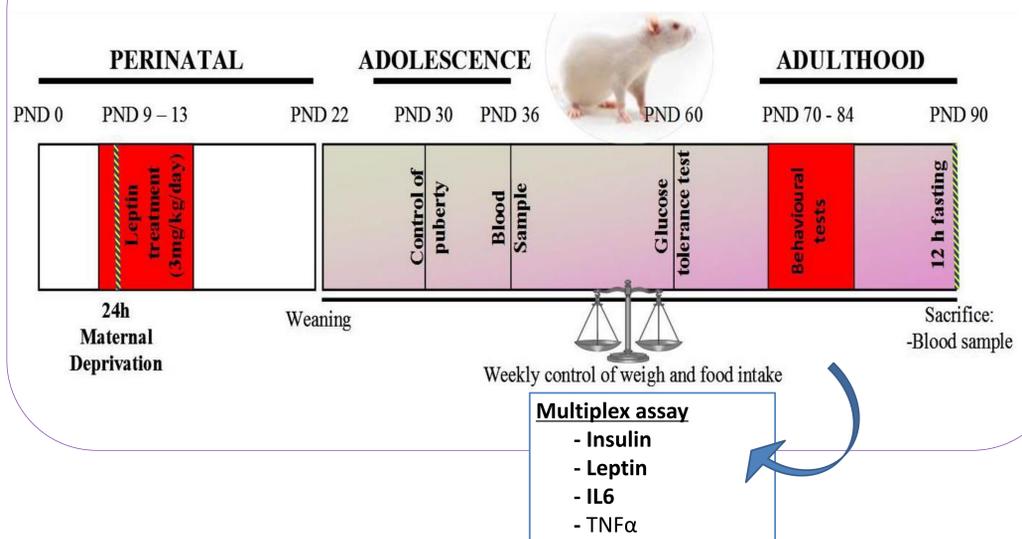
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Introduction

Maternal deprivation (MD) during neonatal life has diverse long-term effects, including modification of metabolism. Some of these effects are sexually dimorphic. We have previously reported that MD in rats blocks the physiological neonatal leptin surge, which could underlie at least some of the long-term metabolic changes.

Hypothesis: We hypothesized that replacement of leptin during MD would normalize long-term endocrine changes.

Methods



Results

Weight and food intake

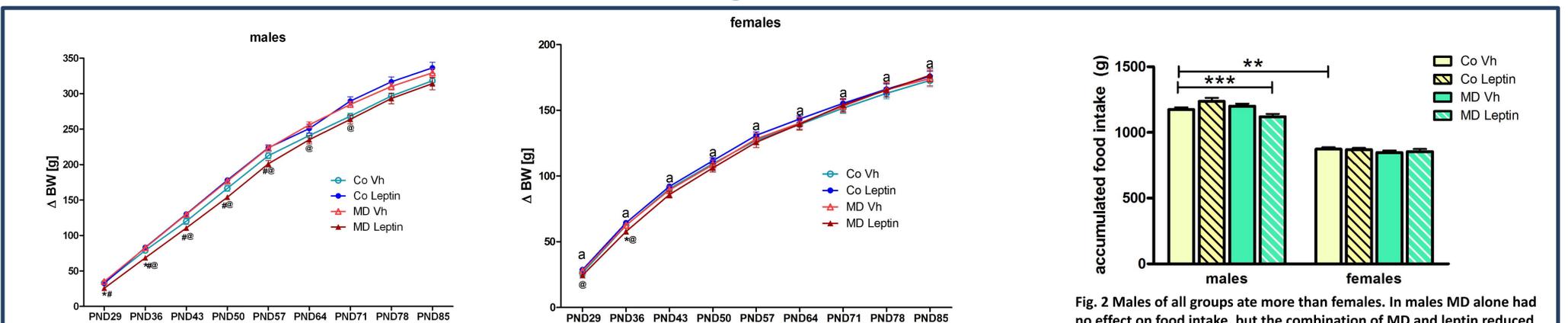


Fig. 1 MD had no significant effect on weight change in either sex. In controls leptin treatment had no effect. Leptin treatment to MD rats reduced weight gain in both sexes with this difference not being found after 75 days of age in males and 40 days of age in females. * vs CoVh; # vs MDVh; @ vs CoLeptin; a vs males

Fig. 2 Males of all groups ate more than females. In males MD alone had no effect on food intake, but the combination of MD and leptin reduced food intake. There was no effect of either treatment in females.

Pubertal onset

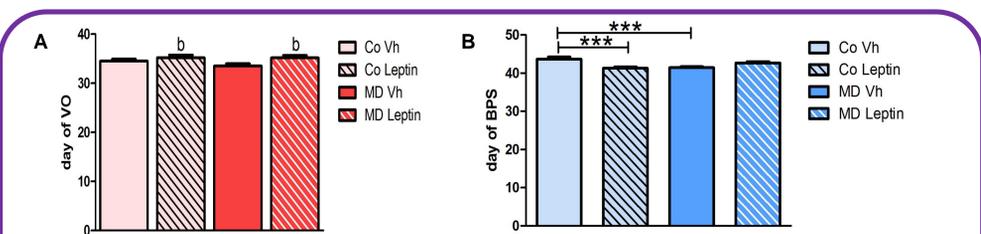


Fig. 3 Neonatal leptin treatment delayed pubertal onset in female rats (A), but advanced it in Co males (B). MD advanced pubertal onset in males, with no effect in females.

Oral glucose tolerance test

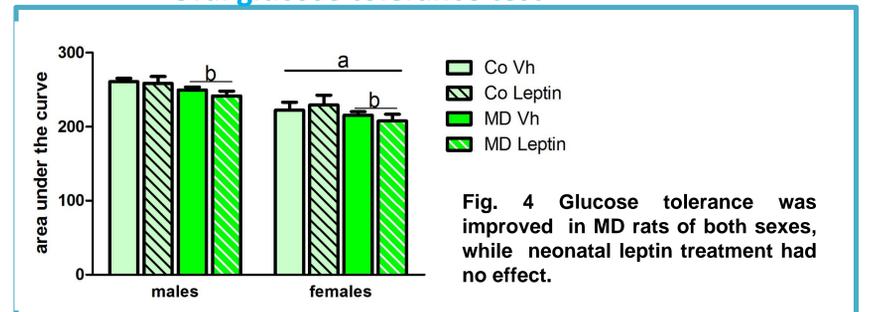


Fig. 4 Glucose tolerance was improved in MD rats of both sexes, while neonatal leptin treatment had no effect.

Serum

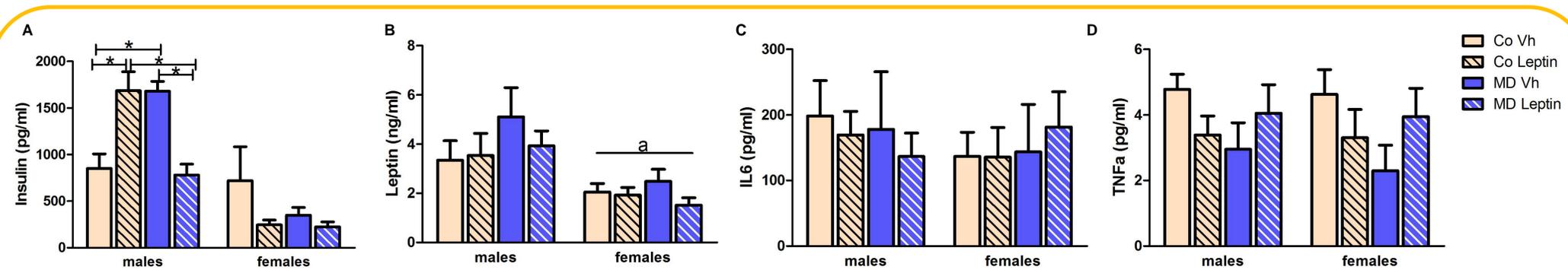


Fig. 5 In males serum insulin levels (A) were increased by MD and neonatal leptin treatment increased them in control animals, but decreased them in MD rats. There was no effect in females. Serum leptin levels (B) were higher in males than in females and were not affected by MD or leptin treatment in either sex. There were no differences between any experimental group in IL6 (C) or TNFα (D) levels. Co Vh: control animals with vehicle; Co Leptin: control animal with leptin treatment; MD Vh: maternal deprivation animals with vehicle; MD Leptin: maternal deprivation animals with leptin treatment.

Three Way ANOVA: (a) main effect of sex; (b) main effect of MD * p<0.05; **p<0.01 and ***p<0.005.

Conclusion

Neonatal leptin treatment of MD rats normalizes some of the endocrine parameters disrupted by this manipulation, but exacerbates other changes. Hence, the factors inducing long-term changes are most likely multiple with diverse interactions.