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α-Calcitonin gene-related peptide protects the vasculature in L-NAME-induced hypertension

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Introduction α-Calcitonin Gene-Related Peptide (αCGRP) is a potent vasodilator neuropeptide that has recently been shown to be protective in AngII-induced hypertension (1). The current study aimed to characterize the L-NAME-induced experimental model of hypertension and elucidate whether αCGRP's protective mechanism involves nitric oxide.

Method All *in vivo* procedures were carried out in accordance to the UK Home Office Animals (Scientific Procedures) Act 1986. Age-matched adult male C57BL/6J wild type (WT) and αCGRP knock-out (KO) mice were used to obtain baseline values of systolic blood pressure (SBP) non-invasively via tail-cuff plethysmography(1), prior to being randomly assigned to receive L-NAME (1mg/ml, Sigma) in their drinking water for 6 weeks. Control groups received tap water. Upon termination; aortic tissues were fixed in 4% paraformaldehyde, processed and embedded in paraffin before 5µm sections were cut and stained with Masson's trichrome to assess vascular remodelling[1]. Data is expressed as mean±SEM (n=5-6) and analysis was performed using two-way ANOVA followed by Bonferroni *post hoc* test.

Results All mice were normotensive at baseline, and the vehicle treated mice maintained normal SBP throughout the study. 2 weeks of L-NAME treatment induced hypertension in WT mice which was found to be statistically significant from vehicle treated WT mice. The αCGRP KO mice developed an increase in SBP, a mean of 138.5 ± 3.9 mmHg, after only one week of receiving 1mg/ml L-NAME treatment which was found to be significantly different ($p<0.05$) to its WT counterpart (121.2 ± 2.7 mm Hg) and this continued from Weeks 3 to 6.

Conclusion Chronic treatment with L-NAME induced exacerbated hypertension in αCGRP KO mice suggesting that αCGRP played a protective role in the L-NAME treated WT mice. Unlike the AngII-induced model, L-NAME treatment did not lead to an increase in heart mass or vascular remodelling in the aorta. However, cell biology profiling remains to be implemented. In conclusion, this study established a model of hypertension and provided novel data supporting an NO-independent protective role of αCGRP, which is distinct from its role previously shown with AngII.

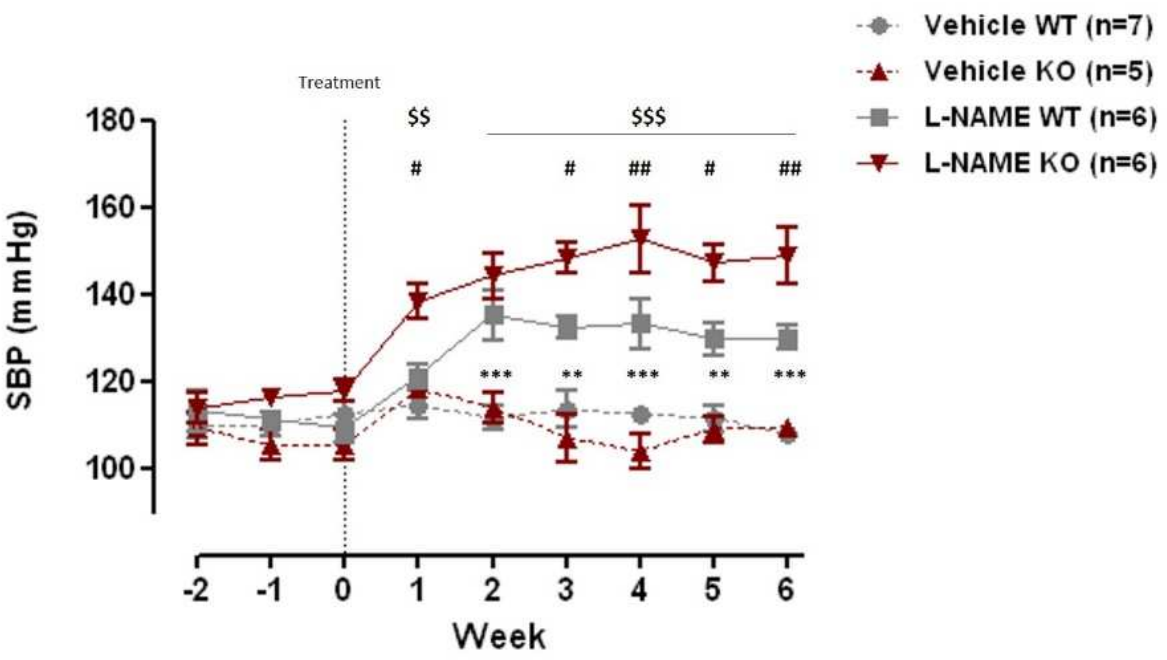

Figure 1 - Effect of 1mg/ml L-NAME treatment on WT and αCGRP KO mice. Mean ± S.E.M. **p<0.01, ***p<0.001 for WT vehicle treated mice vs WT L-NAME treated mice, $$p<0.01, $$$p<0.0001 for αCGRP-KO vehicle treated mice vs αCGRP-KO L-NAME treated mice, #p<0.05, ##p<0.01 for αCGRP-KO L-NAME treated mice vs WT L-NAME treated mice.

References

(1) Smillie SJ *et al.* (2014). *Hypertension* **63**(5): 1056-1062.