

Magnesium Sulphate Treatment During Hypertensive Pregnancy Improves Maternal but not Fetal Outcomes in Rats

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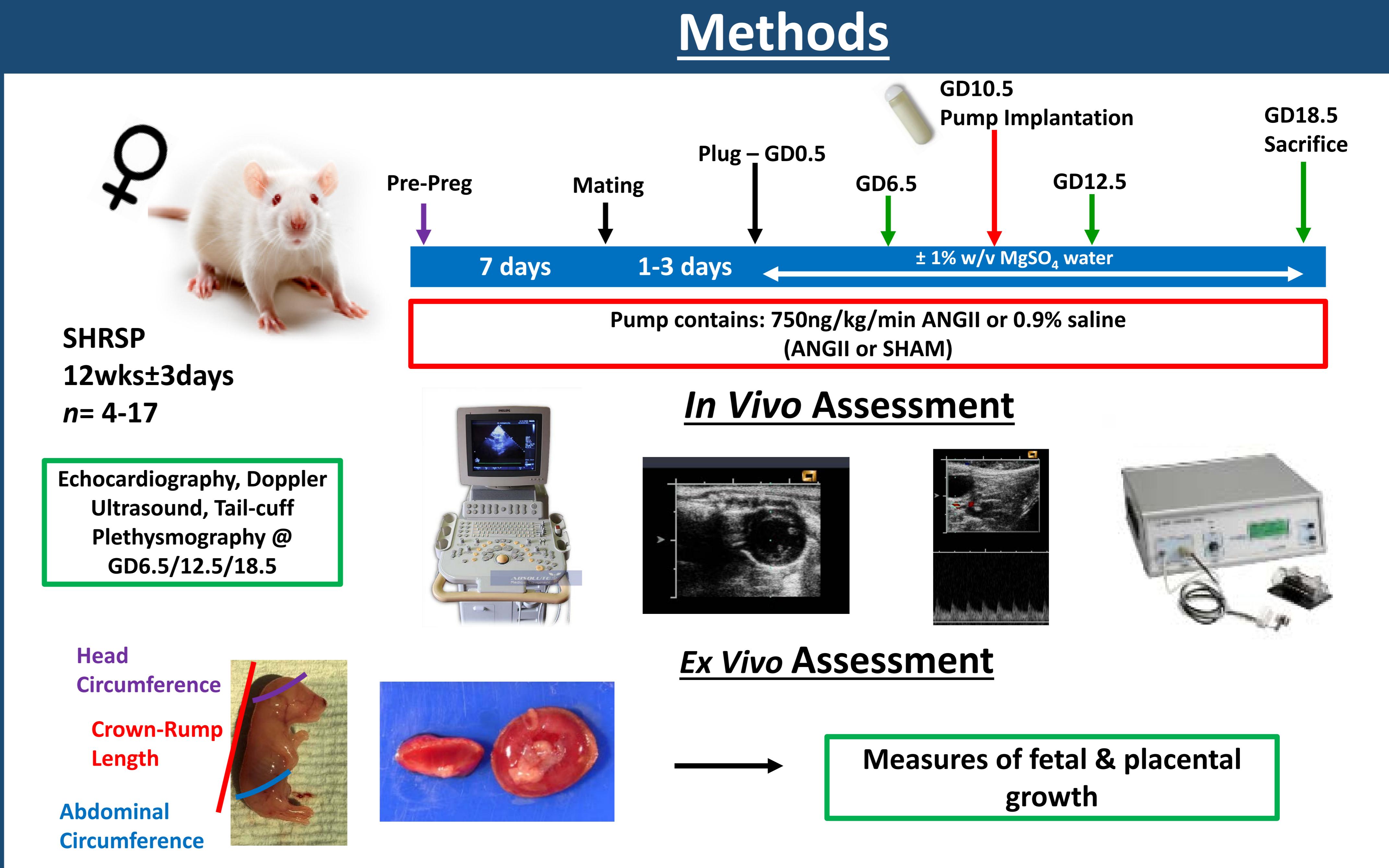
Background

Pre-eclampsia super-imposed on a background of pre-existing hypertension (SPE)¹, is clinically defined as the sudden onset or worsening of proteinuria and/or loss of BP control². This is in part, due to deficiencies in uterine spiral artery vascular remodelling leading to insufficient uteroplacental perfusion and endothelial dysfunction^{2,5}. This results in poor maternal & fetal outcomes¹. There is a current need for new, safe therapeutics in the treatment of SPE. One promising agent is magnesium sulphate ($MgSO_4$), which is known to exert a vasodilatory effect via an increased production of nitric oxide (NO) and thus improving endothelial function⁵. The stroke-prone spontaneously hypertensive rat (SHRSP) is a model of chronic hypertension and defective vascular remodelling during pregnancy that can be stressed by administration of angiotensin II (ANGII) to mimic super-imposed pre-eclampsia⁴. In this study, we utilise 1% w/v $MgSO_4$ in drinking water as a preventative therapeutic and assess its efficacy by phenotypic measurements in this rat model.

Aim

This study aimed to assess the effectiveness of 1% w/v $MgSO_4$ administered in drinking water as a preventative therapeutic for the treatment of super-imposed pre-eclampsia in rats.

Methods



Results

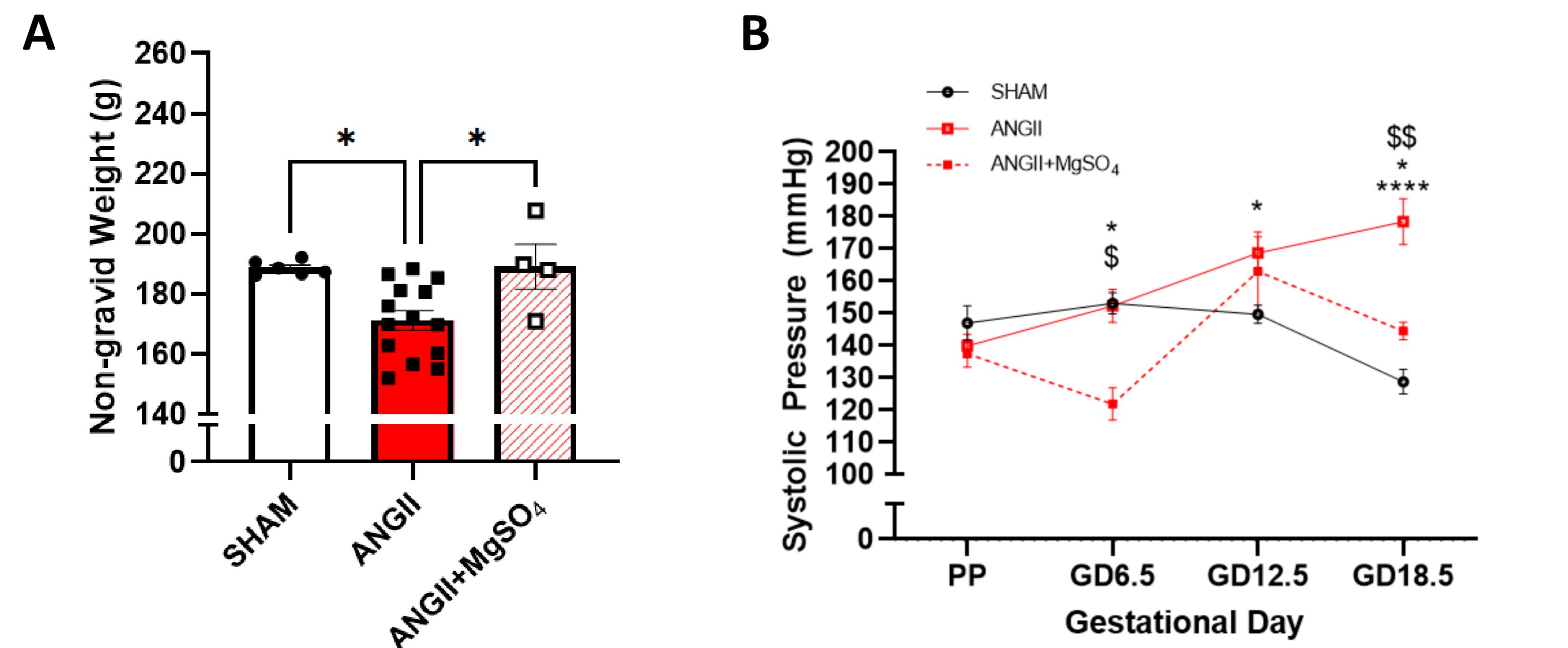


Figure 1: ANGII treatment significantly reduced pregnancy-related weight gain (A) vs SHAM that was restored by $MgSO_4$. There was also a significant increase in systolic blood pressure (B) following ANGII infusion at GD10.5 that was not sustained in the ANGII+ $MgSO_4$ group.

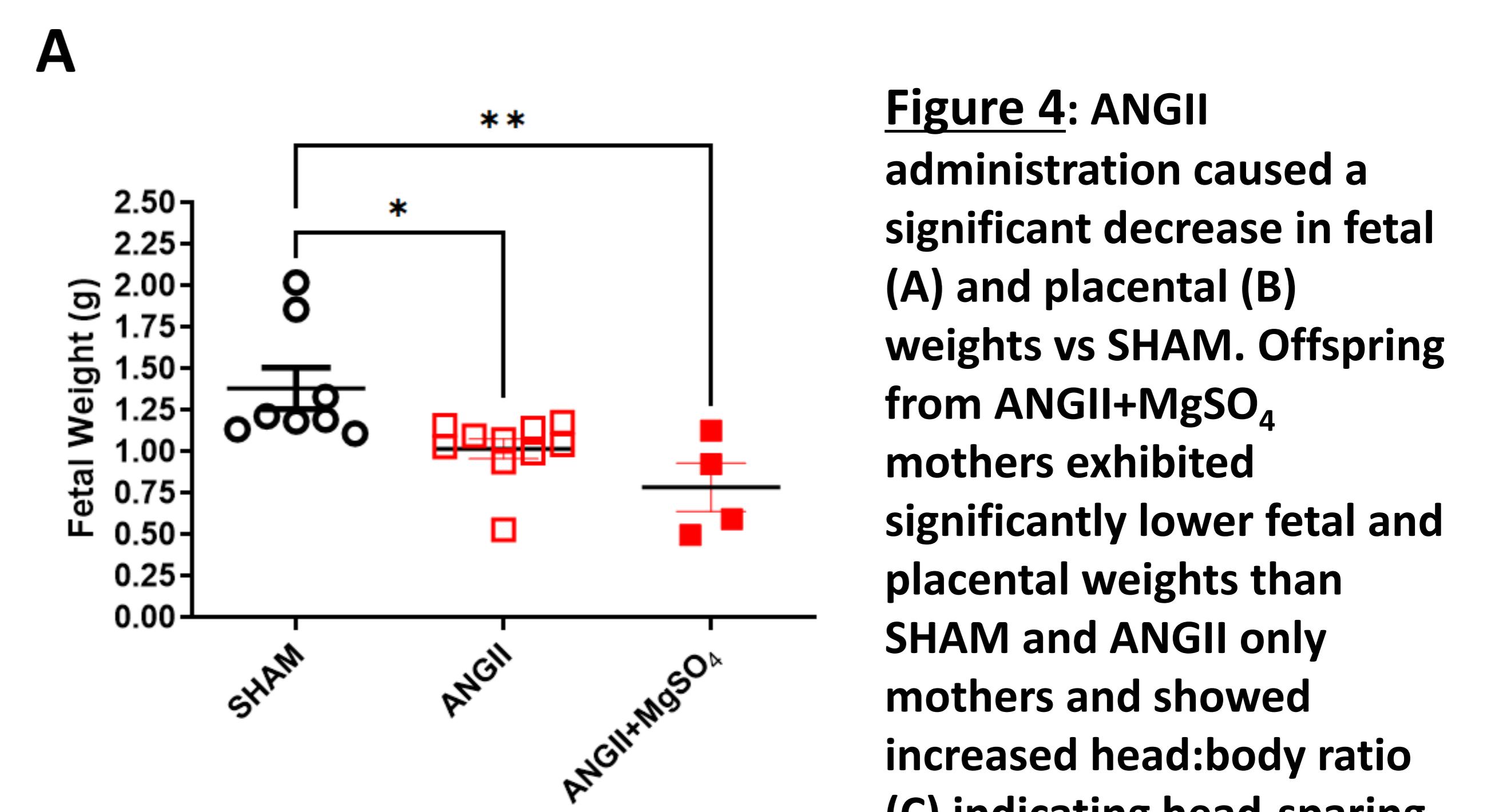


Figure 4: ANGII administration caused a significant decrease in fetal (A) and placental (B) weights vs SHAM. Offspring from ANGII+ $MgSO_4$ mothers exhibited significantly lower fetal and placental weights than SHAM and ANGII only mothers and showed increased head:body ratio (C) indicating head-sparing growth restriction *in utero*.

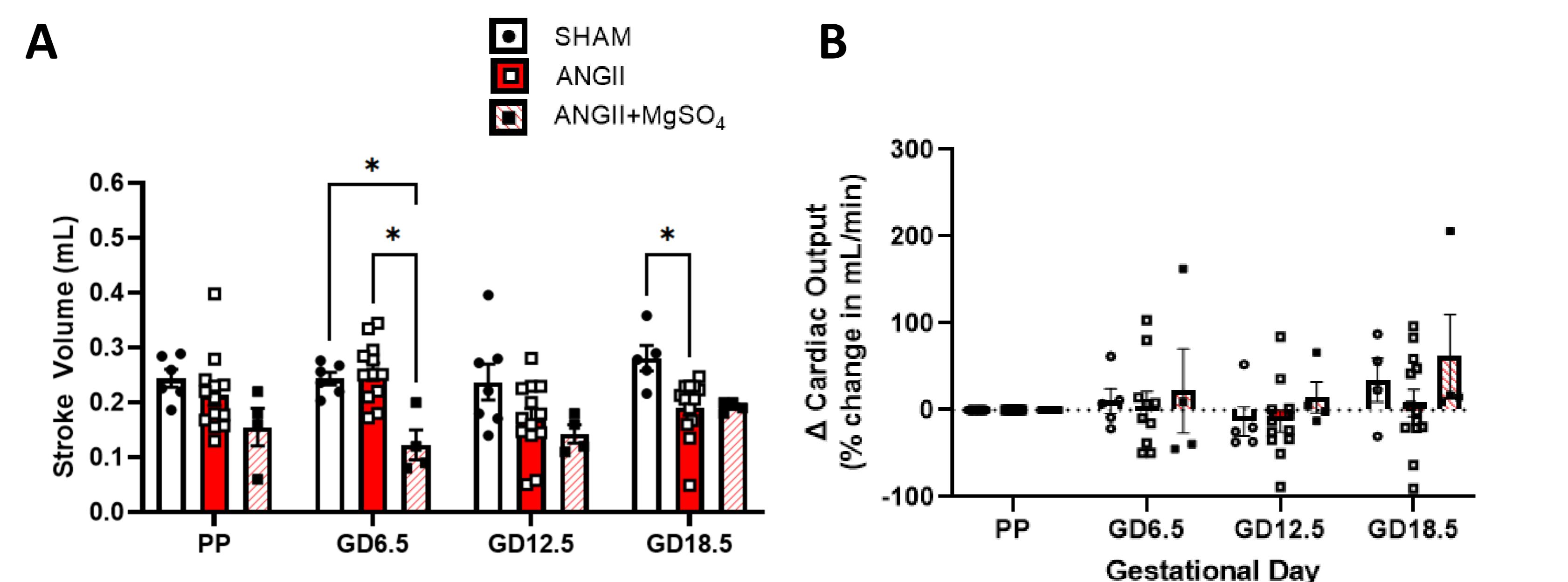


Figure 2: ANGII treatment induced cardiac dysfunction in the left ventricle as measured by decreased stroke volume (A) and cardiac output (B). Treatment with $MgSO_4$ appeared to increase SV throughout gestation as well as improve cardiac function relative to baseline at pre-pregnancy.

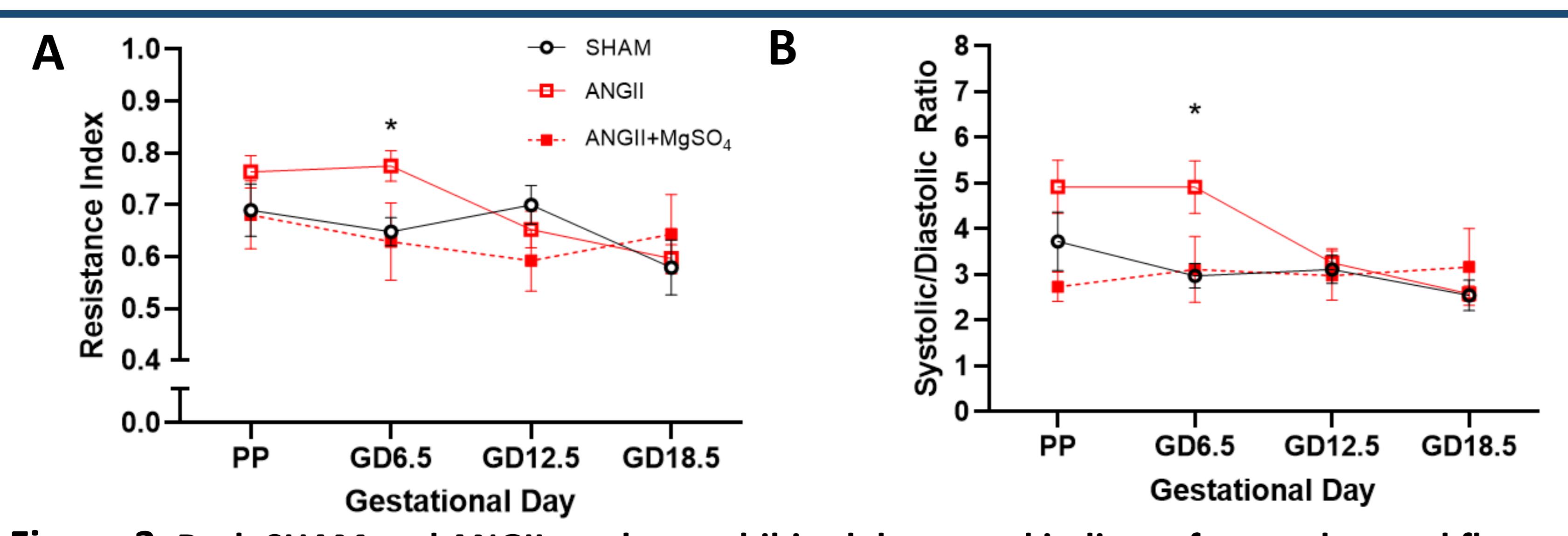


Figure 3: Both SHAM and ANGII mothers exhibited decreased indices of uteroplacental flow - resistance index (A) and systolic/diastolic ratio - at GD18.5. 1% $MgSO_4$ drinking water had no effect on uteroplacental flow.

Summary & Conclusions

- Administration of 750ng/kg/hr ANGII significantly impacts maternal cardiovascular function and fetal growth during pregnancy in SHRSP dams.
- Treatment with 1% w/v $MgSO_4$ drinking water significantly improves both maternal weight gain and systolic blood pressure throughout pregnancy.
- There is evidence to suggest that $MgSO_4$ may improve maternal left ventricular cardiac dysfunction in this model, however more n numbers are required to fully understand this effect.
- Despite its vascular actions, $MgSO_4$ therapy does not improve indices of uteroplacental blood flow.
- By contrast, we found $MgSO_4$ to be detrimental to fetal development, shown by significantly reduced fetal and placental weights and increased head:body ratio vs both SHAM and ANGII only offspring.

This data shows that magnesium sulphate may be beneficial for maternal but not fetal outcomes in a rat model of super-imposed pre-eclampsia, however further work is required to confirm this finding.

References

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4. Small et al (2016). Placenta. 37:1.
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