

EFFECT OF CHRONIC NICOTINE EXPOSURE ON MATERNAL ADAPTATIONS TO PREGNANCY IN RATS

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INTRODUCTION

Pregnancy is characterized by adaptations of the maternal organism including systemic and intrarenal vasodilatation with elevations in renal plasma flow (RPF) and glomerular filtration rate (GFR), with increased sodium and water reabsorption.

Nicotine displays opposite renal effects such as reduction of RPF, GFR and increased renal vascular resistance.

The effects of nicotine on fetal development has been widely studied, however, few studies are directed to its effects on the maternal adaptation to pregnancy.

The effects of nicotine in the tubular transport during pregnancy are not known.

OBJECTIVES

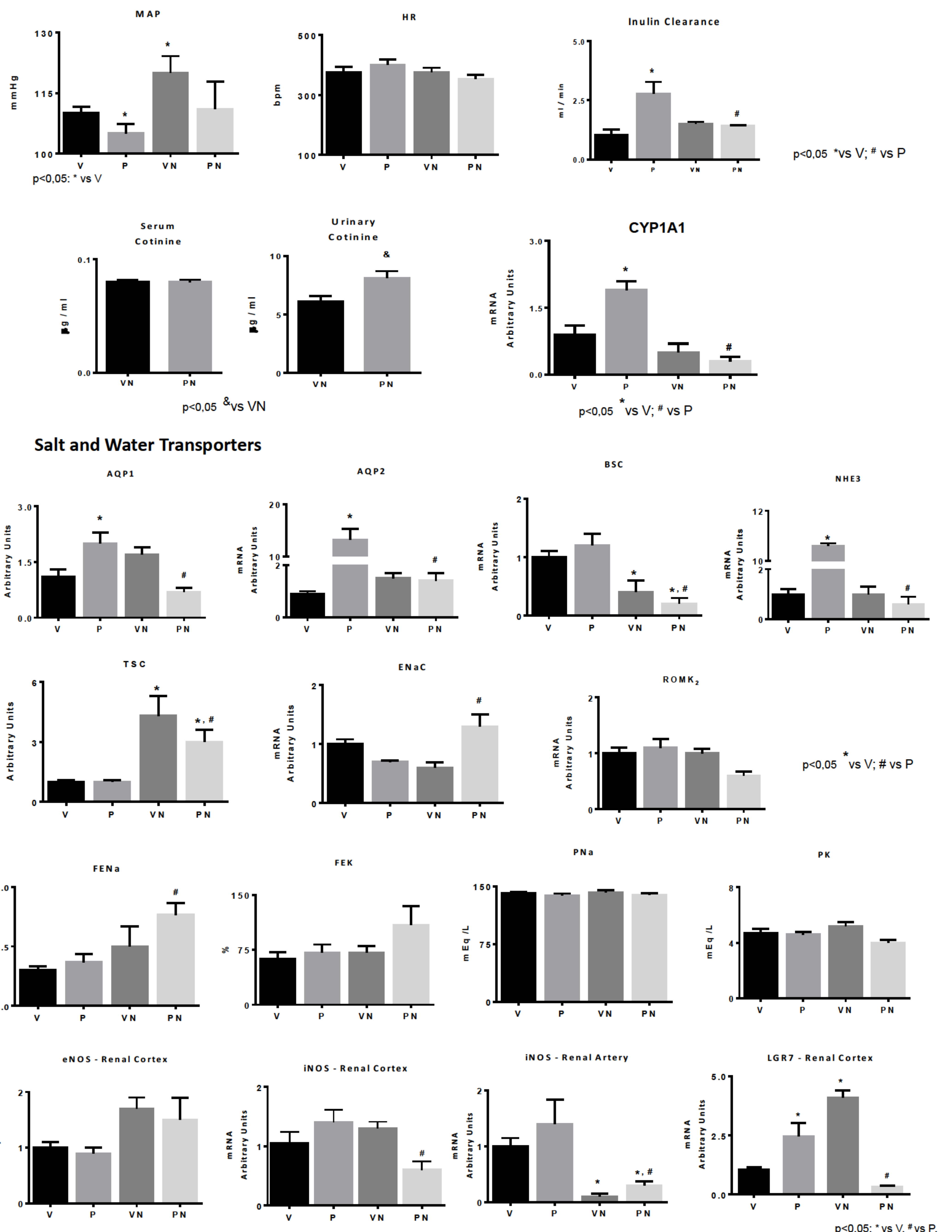
- To evaluate the effects of nicotine, continuously administered, before and during pregnancy on maternal blood pressure and renal function.
- To assess whether nicotine interferes with the expression of tubular water and electrolytes transporters.
- To evaluate the expression profile of hormonal pathways involved in the adaptation to pregnancy such as relaxin receptors and nitric oxide (NO) pathway.

METHODS

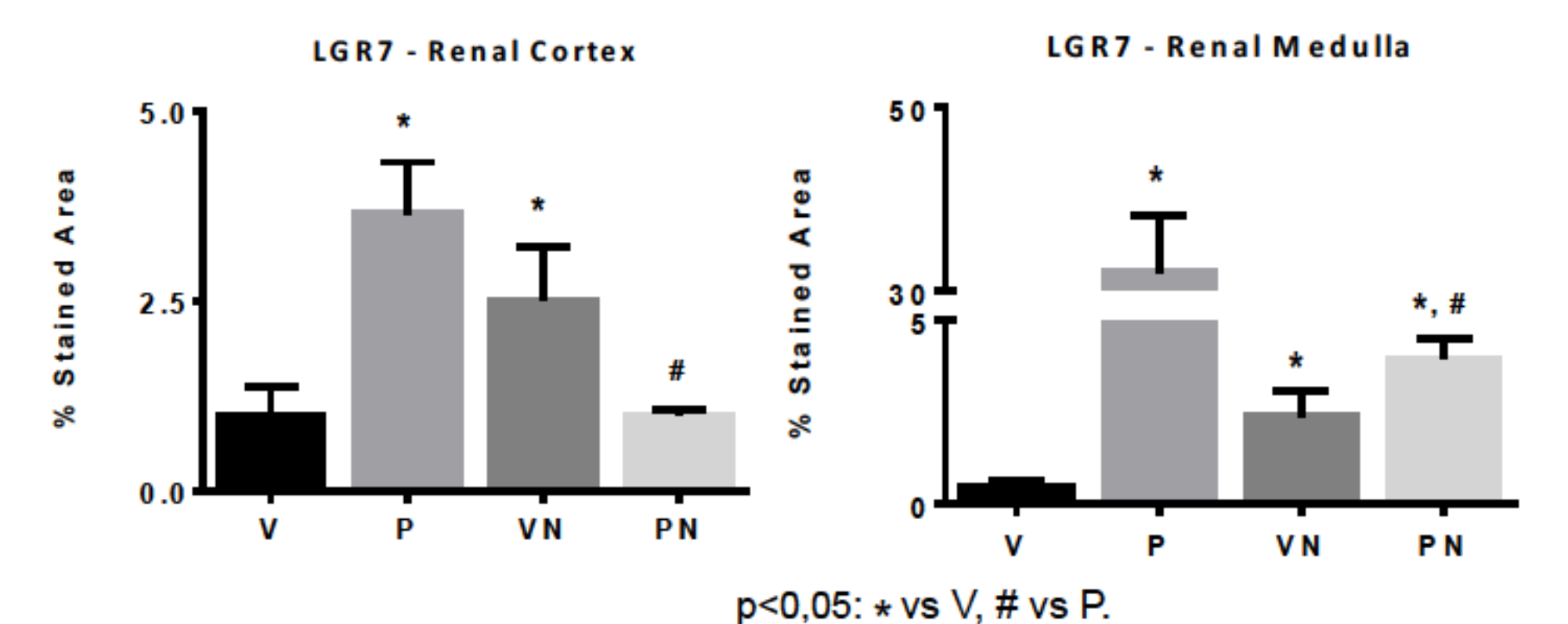
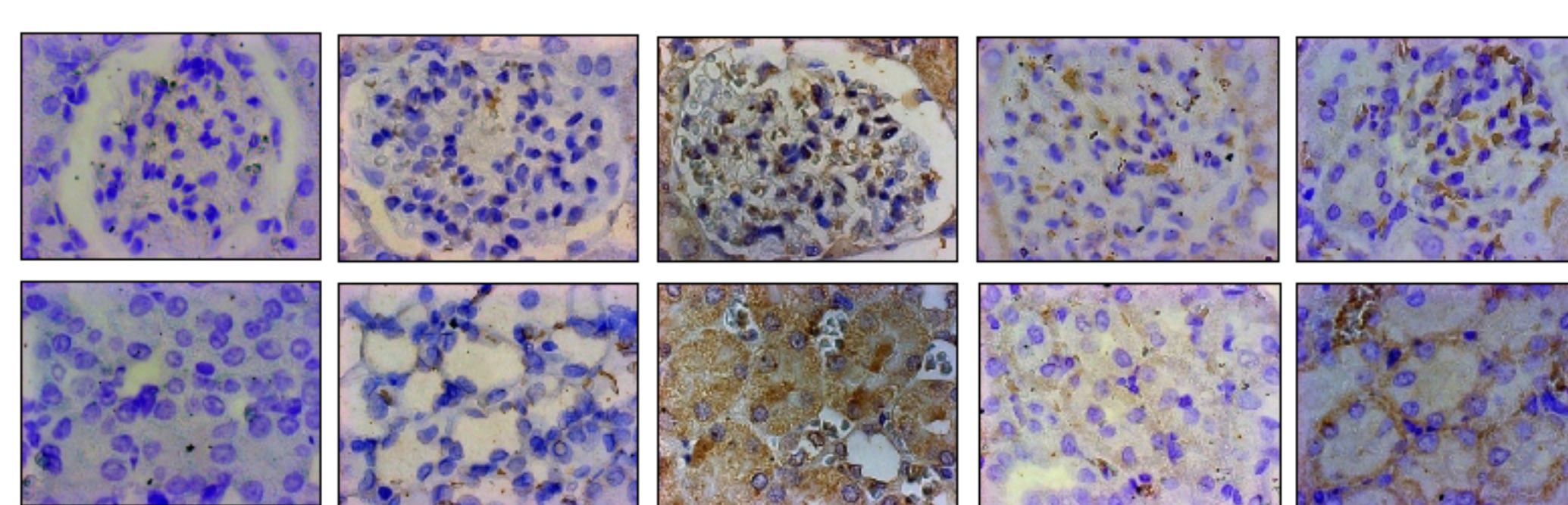
- Adult female Wistar rats were allocated into groups: Virgin (V) and pregnant (P).
- Nicotine (6 mg/k/day) or saline were administered through osmotic mini pumps implanted subcutaneously, during 28 days.
- In pregnant animals treatments started 14 days before pregnancy induction and during 14 days after conception.

Parameters evaluated:

- Systemic: MAP, heart rate.
- Biochemical: plasma and urine cotinine, Na⁺ and K⁺ excretion.
- Inulin clearance by fluorescent method.
- Expression levels of the main tubular transporters, nicotine metabolizing enzyme (CYP1A1), iNOS, eNOS and relaxin receptor (LGR7) were determined by real time PCR and/or immunostaining.



LGR7 in renal tissue



SUMMARY AND CONCLUSION

Exposure of pregnant rats to nicotine caused:

- The reduction in MAP, typical of the pregnancy, was abolished by nicotine.
- Increased FENa, as a result of downregulation in the major Na⁺ transporters in the proximal nephron, which could impair Na⁺ retention during pregnancy.
- Reduction in the expression of AQP1 and AQP2 contributing to impair the typical extracellular volume expansion of the pregnancy.
- Reduction in GFR and increased proteinuria.
- Reduction in renal expression of iNOS enzyme and relaxin receptors.

In conclusion, this study showed that chronic exposure of pregnant rats to nicotine caused deleterious effects that were beyond to those observed in virgin rats. These effects can potentially result in negative influences on the systemic and renal adaptations of the maternal organism to pregnancy.

