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Neonatal Expression of the GPR12 Receptors in Rat Model of Prenatal Hypoxia

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INTRODUCTION

Pre-neonatal Hypoxic Ischemic (HI) is asphyxia of the umbilical blood supply to the human fetus at 36 gestational weeks or later. The prenatal period is one of the crucial periods for neonatal brain formation. Given the importance of G-protein coupled receptors (GPCRs) as the main target for several drugs that can control some CNS diseases, the need to study the involvement of GPCRs in the pathophysiology of prenatal hypoxia is crucial. One of the highly expressed GPCRs in the CNS is G-Protein coupled receptor 12 (GPR12). This orphan GPCR plays a role in neuronal development, differentiation, and synaptic and neurite formation. Therefore, this study aims to assess the effect of prenatal hypoxia in the expression of GPR12 in neonatal rats.

OBJECTIVES

Assessing the effect of intrauterine hypoxia on the brain histology.

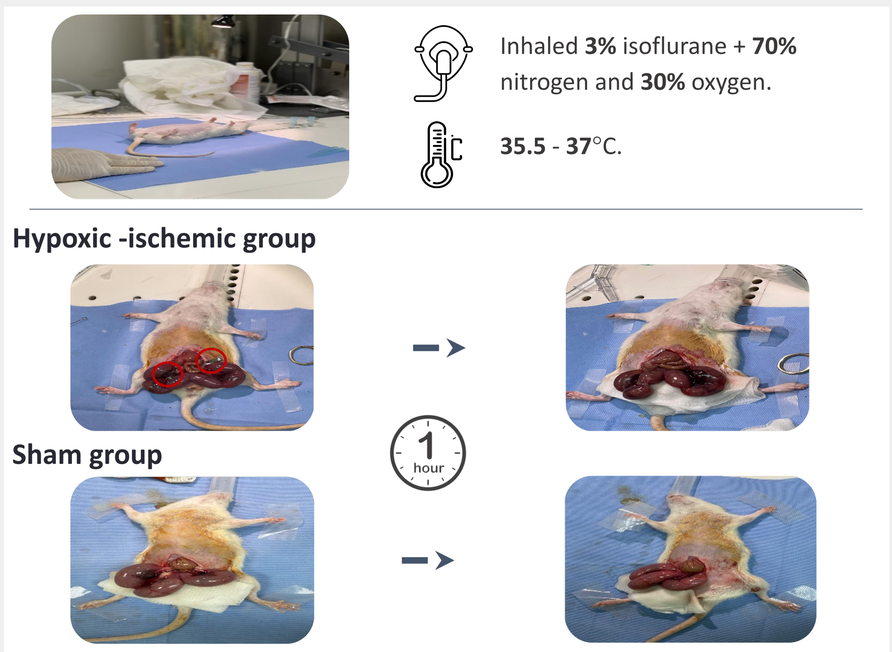
Assessing the effect of intrauterine hypoxia on the expression of GPR12 on protein levels.

Measuring the changes in the protein levels of GFAP.

METHODS

- **Inducing Transient Hypoxia-Ischemia:**

Four E18 pregnant Sprague Dawley rats, were divided into HI and sham group.



After normal delivery of the pups, samples of their brains were collected and kept in 10% formaldehyde.

- **Histopathological Examination:**

The FFPE brain sections were stained with hematoxylin and eosin, as Berger et al. (2019) described.

- **Immunohistochemistry**:

The immunoreactivity signals of the GPR12 receptor and GFAP were assessed in FFPE as described by Kozielewicz et al. (2017).

- **Statistical Analysis:**

The difference between the groups was analyzed using Student's T-test, performed using Prism 8. P-value equal to ≤ 0.05 is considered significant.

RESULTS

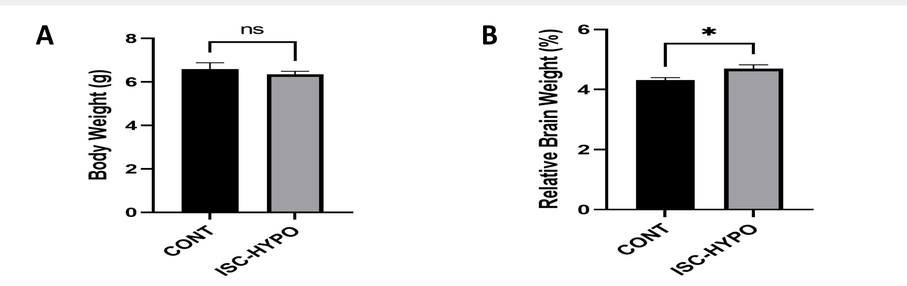


Figure 1: The body weight and the relative changes in the brain weight between ischemic-hypoxia and sham groups. **A:** body weight, **B:** relative brain weight, indicating brain edema. The data represented as mean ± SEM (n = 16, *$p < 0.05$)

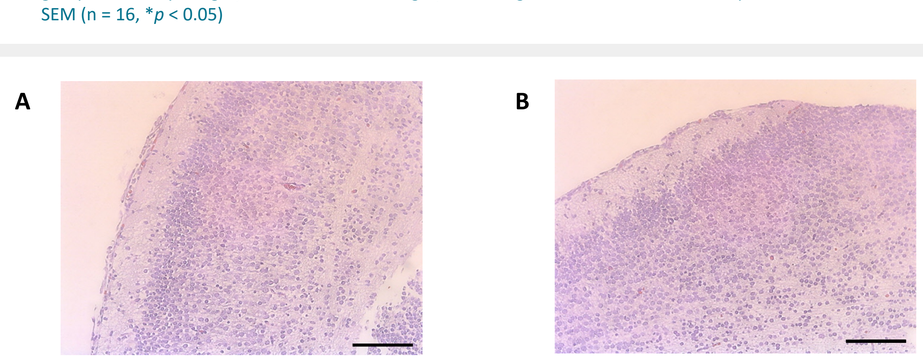


Figure 2: Unremarkable histological alterations in the cortex of neonatal ischemic-hypoxic rat brain. **A:** control group, **B:** prenatal ischemic-hypoxia group. (n = 8-9, scale bar = 20 µm).

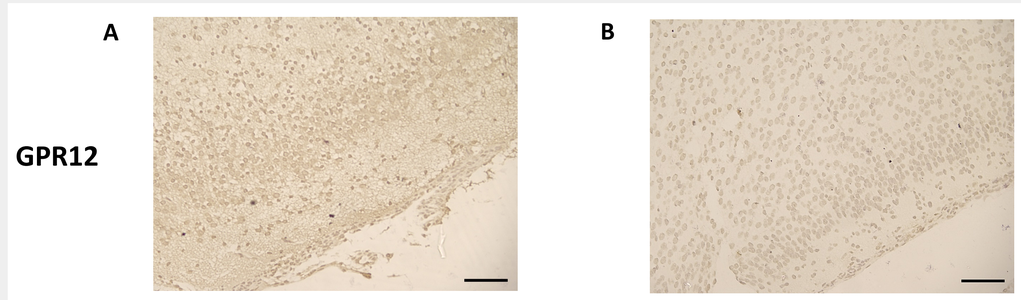


Figure 3: Immunoreactivity signals of GPR12 protein in the cortex of neonatal rat brains pre-exposed to prenatal ischemic-hypoxia. Mild to moderate downregulation of GPR12 IR in the disease group. **A:** control group, B: prenatal ischemic-hypoxia group. (n = 8-9, scale bar = 20 µm).

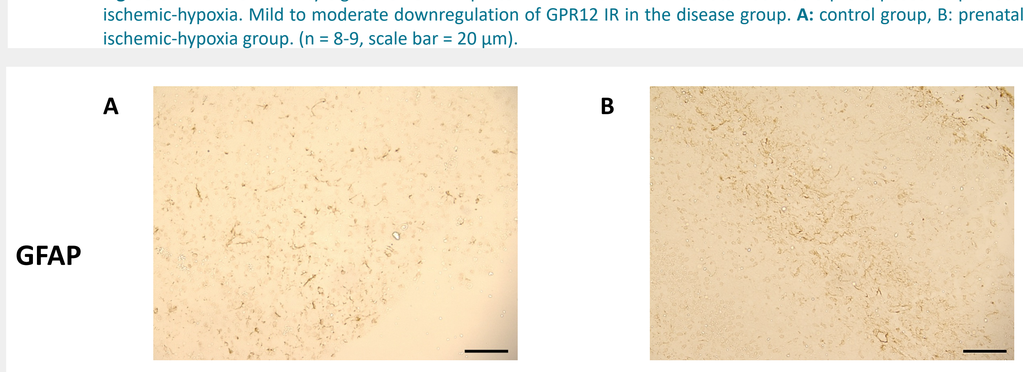


Figure 4: Immunoreactivity signals of GFAP protein in the cortex of neonatal rat brains pre-exposed to prenatal ischemic-hypoxia. Upregulation of GFAP signals in the disease group indicates astrocytosis. **A:** control group, **B:** prenatal ischemic-hypoxia group. (n = 8-9, scale bar = 20 µm).

DISCUSSION & CONCLUSIONS

GPR12 plays a role in neurite outgrowth and axonal regeneration. Since prenatal hypoxia resulted in impaired neurotransmitter circuits and synaptic plasticity in the brain cortex, this might explain the decrease of GPR12 levels in the cerebral cortex. Hence, GPR12 can be used as a research tool and potentially developed into a target for therapeutic agents with a new mechanism of action.

REFERENCES

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