SEXUAL DIMORPHISM OF IGF1 AND IGF2 EXPRESSION IN THE NEONATAL RAT BRAIN

Santiago Guerra-Cantera[1, 2, 3,*], Marta Torrecilla-Parra [2], Francisca Díaz[1, 3], Jesús Argente[1, 2, 3, 5], Julie A. Chowen[1, 3]

[1] Department of Endocrinology, Hospital Infantil Universitario Niño Jesús, Instituto de Investigación La Princesa, Madrid, Spain. [2] Department of Pediatrics, Universidad Autónoma of Madrid, Madrid, Spain. [3] Centro de Investigación Biomédica en Red de la Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III, Madrid, Spain. [4] Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain. [5] IMDEA Food Institute, CEI UAM + CSIC, Madrid, Spain.
* email: santiguerra8@gmail.com

INTRODUCTION

Insulin-like growth factor (IGF) 2 plays a fundamental role in prenatal growth and development. The *IGF2* gene is imprinted, with the paternally inherited copy being active and the maternal copy being silenced in most tissues. During development, the expression of IGF2 is sexually dimorphic in some tissues and this is thought to be involved in the development of some sexually dimorphic features. For example, IGF2 expression is reported to be higher in the male brain compared to females, but less is known regarding specific brain areas and cell types. As the hypothalamus is implicitly implicated in the control of sexually dimorphic endocrine functions and glial cells participate in this control, we asked whether their expression of IGF2 and other members of the IGF system are sexually dimorphic.

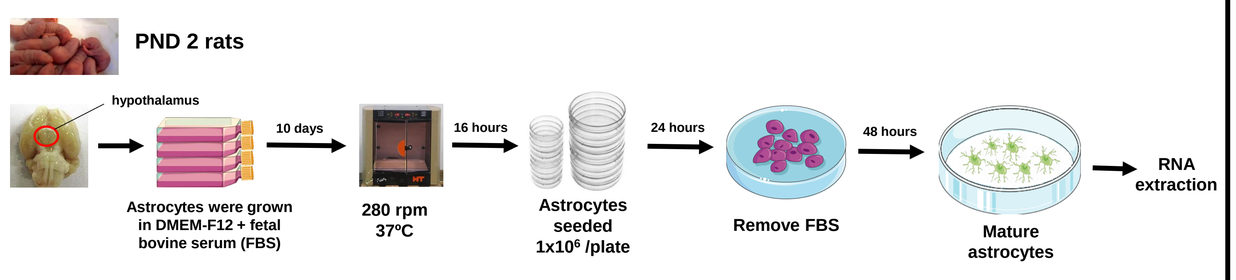
OBJECTIVES

1) Determine if the overall expression of IGF2 is sexually dimorphic in specific brain regions, including the hypothalamus.
2) Compare the expression of the IGF system in hypothalamic astrocytes from male and female neonatal rats.

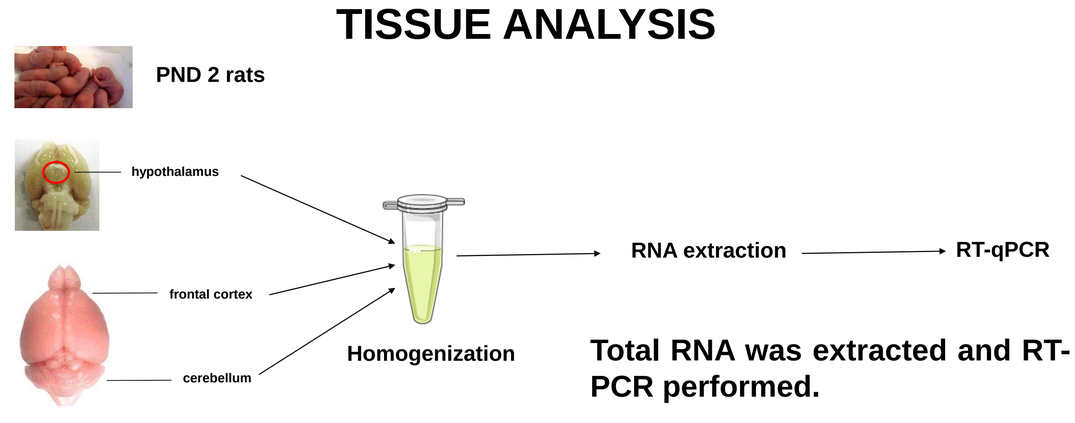
MATERIAL AND METHODS

PRIMARY HYPOTHALAMIC ASTROCYTE CULTURES

Primary hypothalamic astrocyte cultures were prepared from PND 2 male and female Wistar rats and grown under standard conditions for 10 days.



TISSUE ANALYSIS



Total RNA was extracted and RT-PCR performed.

RESULTS

HYPOTHALAMIC ASTROCYTE CULTURES

In hypothalamic astrocyte cultures, IGF1 expression was higher in males ($p<0.01$) and IGF2 expression higher in females ($p<0.05$). Expression of IGF2R tended to be higher in females and IGF1R in males, but these differences did not reach statistical significance.

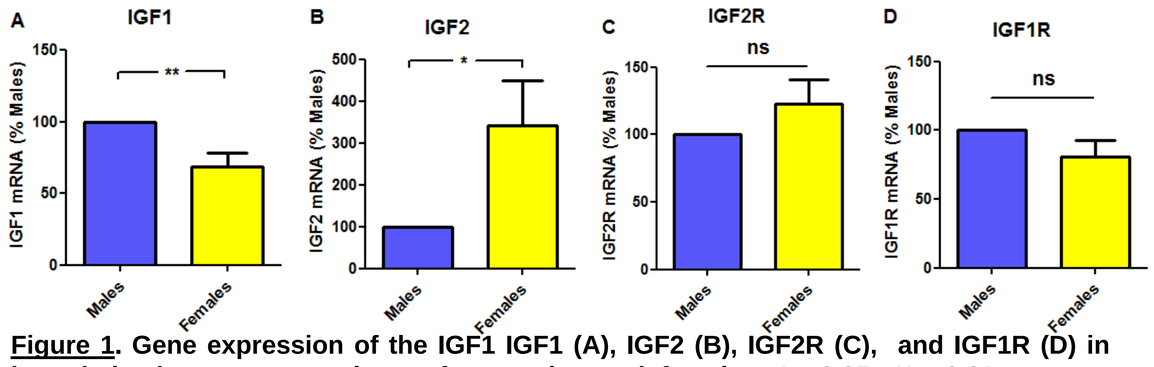


Figure 1. Gene expression of the IGF1 IGF1 (A), IGF2 (B), IGF2R (C), and IGF1R (D) in hypothalamic astrocyte cultures from males and females. *p<0.05; **p<0.01. ns=non significant. Data are represented by mean ± SEM. N = 6.

None of the remaining IGF family members analyzed [pregnancy-associated plasma protein-A, IGF-binding proteins (IGFBP) 2, 3, 4 and 5 and stanniocalcin (STC) -2] differed between the sexes at this age.

	Males	Females
PAPP-A	100 ± 0.0	90.97 ± 12.2
IGFBP2	100 ± 0.0	91.34 ± 12.0
IGFBP3	100 ± 0.0	105.42 ± 22.5
IGFBP4	100 ± 0.0	91.02 ± 16.0
IGFBP5	100 ± 0.0	134.61 ± 41.0
STC-2	100 ± 0.0	92.99 ± 30.0

Table 1. Gene expression of IGF1 system components in hypothalamic astrocyte cultures that did not differ between males and females. Data are represented by mean ± SEM. N=3.

TISSUE ANALYSIS

CEREBELLUM

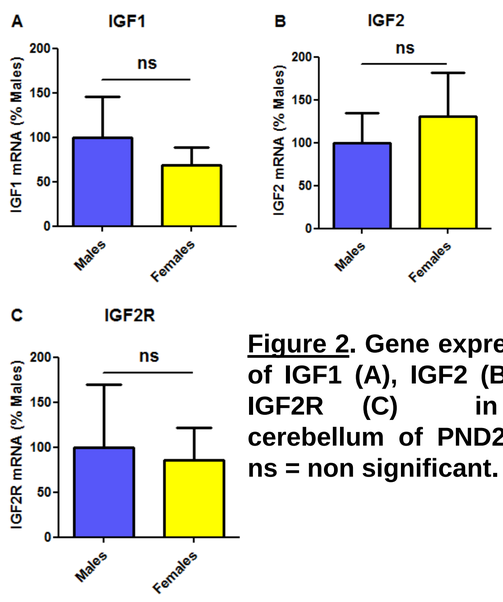


Figure 2. Gene expression of IGF1 (A), IGF2 (B) and IGF2R (C) in the cerebellum of PND2 rats. ns = non significant. N=3.

FRONTAL CORTEX

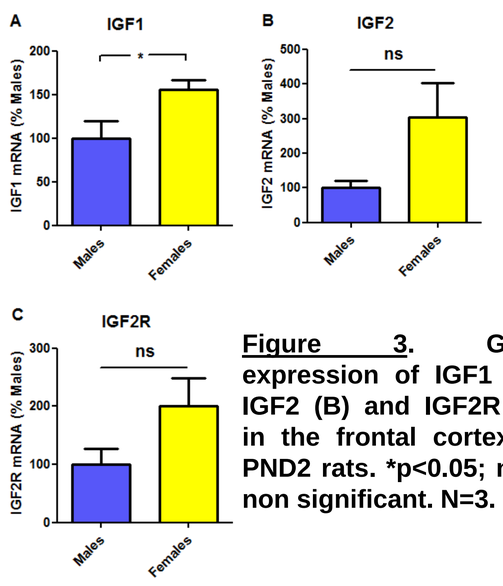


Figure 3. Gene expression of IGF1 (A), IGF2 (B) and IGF2R (C) in the frontal cortex of PND2 rats. *p<0.05; ns = non significant. N=3.

HYPOTHALAMUS

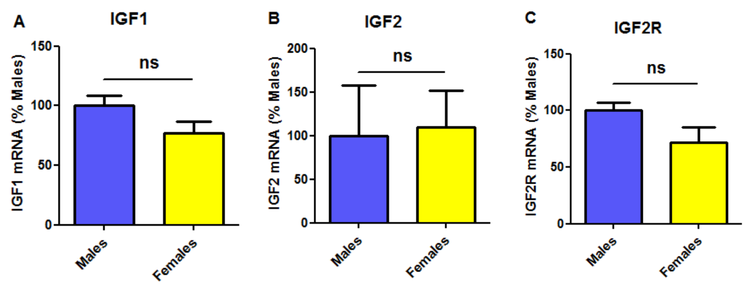


Figure 4. Gene expression of IGF1 (A), IGF2 (B) and IGF2R (C) in the hypothalamus of PND2 rats. Ns = non significant. N=3.

CONCLUSIONS

1. Expression of IGF1 and IGF2 by hypothalamic astrocytes differs between neonatal males and females, which could participate in the development of sexually dimorphic neurendocrine systems.

2. It remains to be determined if this sex difference in IGF expression by astrocytes is age and anatomically specific.

Topic: Fetal, neonatal endocrinology and metabolism

ACKNOWLEDGEMENTS
This work was funded by: MINECO (BFU2014-51836-C2-2), FIS (PI16/00485), Fondos FEDER and CIBEROBN