Study of the sexual dimorphism in the cell death pattern in brains of a model of newborn piglets exposed to hypoxia-ischemia

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Introduction

Perinatal asphyxia is one of the most important causes of morbidity and mortality in newborns, causing 25% of total neonatal mortality. (1)

The neonatal brain is sexually dimorphic in structure and function and, following perinatal asphyxia, sex differences in both factors have been reported.

Material and Methods

15 piglets (9 females and 6 males) were subjected to a quantified global cerebral hypoxic-ischemic insult. At 48 hours after hypoxia-ischemia, the number of necrotic, apoptotic and caspase-3 positive cells was quantified in five brain regions of both neonatal female and male pigs.

Objective

To study the possible existence of a sexual dimorphism in the pattern of cell death in the brain of new-born piglets after neonatal asphyxia.

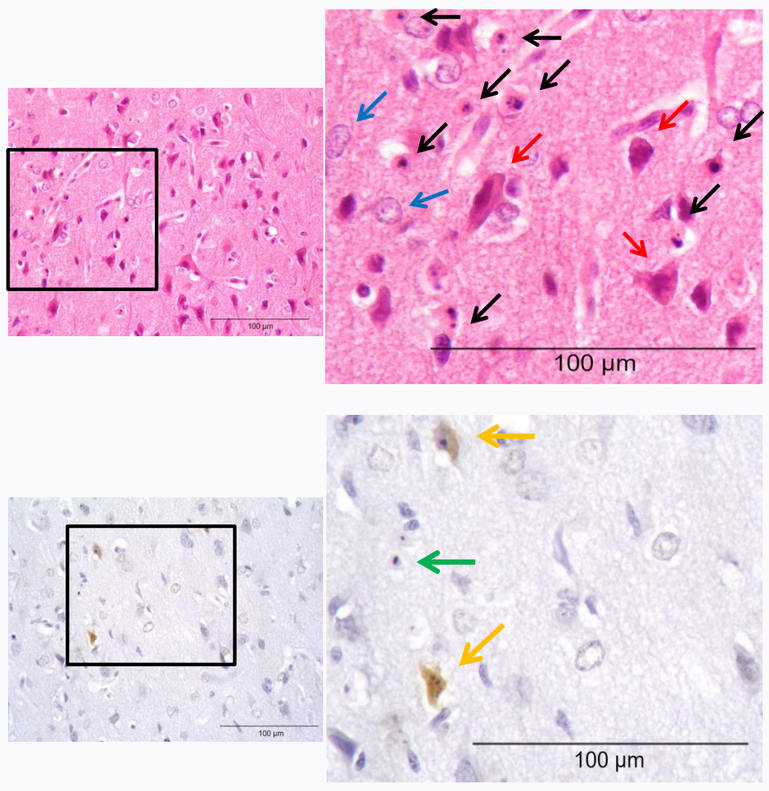

***Figure 1**. Images of haematoxylin and eosin staining (top) and immunohistochemistry for Caspase-3 (bottom) of the Cingulate Cortex of a sample from a female piglet brain. Original photographies were taken at 400X. Scale Bar: 100 µm. Blue arrow: Well-preserved cell; Black arrow: Apoptotic cell; Red arrow: Necrotic cell; Green Arrow: Apoptotic non-positive Caspase-3 cell. Yellow arrow: Apoptotic Caspase-3 positive cell.*

Results

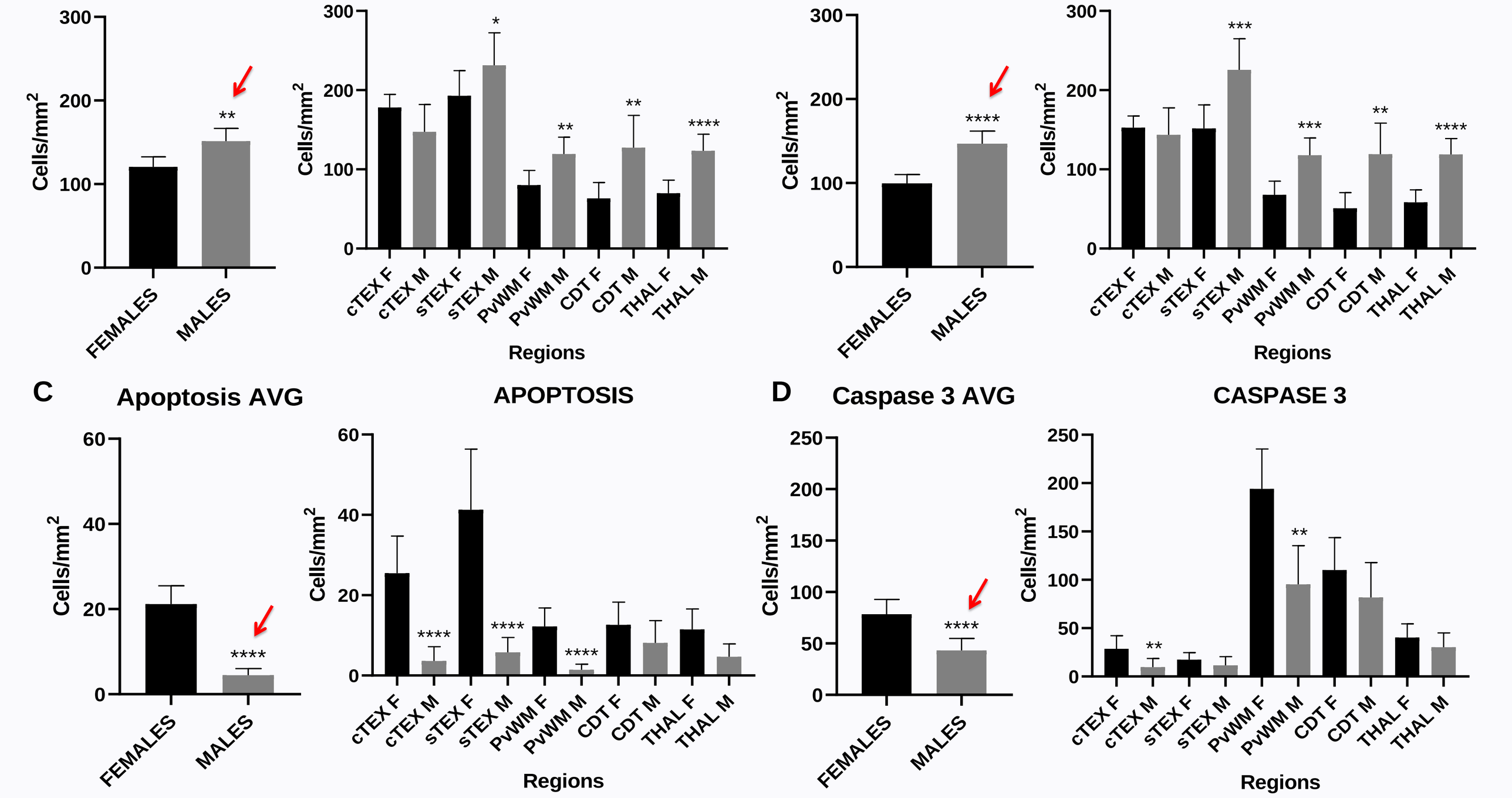

***Figure 2**. Quantification of necrotic, apoptotic, and caspase-3 positive cells in 5 brain regions after hypoxic-ischemic damage in female and male newborn pigs. Females have been represented in black and males in gray. The number of cells has been represented with the Average ± 95% Confidence Interval (CI). A) Cell death. B) Necrosis. C) Apoptosis. D) Caspase-3. Statistical significance: * p <0.05, ** p <0.01, *** p <0.001, **** p <0.0001. cTEX: Cingulate Cortex, sTEX: Sensorimotor Cortex, PvWM: Periventricular White Matter, CDT: Caudate Nucleus, THAL: Thalamus. Red arrows: Statistical significant differences in averages graphs.*

Conclusions

Our results suggest a sexual dimorphism related to the pattern of cell death after neonatal hypoxia-ischemia in piglets, with more cell death and more necrosis in males and more apoptosis in females. Also, we suggest that apoptosis is predominantly via the Caspase-dependent pathway in females. These data open the door to future more individualised and precise therapies, taking into account the brain region and the sex of the new-borns for their treatment.

References. 1. van Bel, F., & Groenendaal, F. (2020). 3, 3–3.