Hypothalamic astrogliosis in adult rat programmed by maternal exposure to nicotine during lactation

Viviane Younes-Rapozo\textsuperscript{1,2}, Filippo Cortes Giovanelli\textsuperscript{1}, Cintia Rodrigues Pinheiro\textsuperscript{1}, Alex Christian Manhães\textsuperscript{2}, Egberto Gaspar de Moura\textsuperscript{1}, Elaine de Oliveira\textsuperscript{1}, Patricia Cristina Lisboa\textsuperscript{1}.

Introduction: Maternal exposure to nicotine during lactation causes hyperleptinemia in the neonate pups and, at adulthood, these animals are overweight and hyperleptinemic, while, in their hypothalamus, the leptin signalling pathway is reduced, evidencing a central leptin resistance. As expected, this is followed by a higher expression of orexigenic Neuropeptide Y and lower anorexigenic neuropeptide cocaine and amphetamine-regulated transcript (CART) expression in the paraventricular nucleus of hypothalamus (PVN). Obesity and hyperleptinemia is close related to hypothalamic inflammation and astrogliosis, characterized by alterations in astrocyte morphology with thickening of processes and increasing of glial fibrillary acidic protein (GFAP) expression.

Goals: Therefore, our goal is to evaluate whether the adult obese animals programmed by maternal nicotine exposure presents hypothalamic inflammation, indicated by astrogliosis.

Methods: On the 2nd postnatal day (P2), dams were subcutaneously implanted with osmotic minipumps releasing nicotine (NIC-6mg/Kg/day) or saline for 14 days (CEUA/017/2012; CEUA/019/2014). Offspring were killed in P180 (n=6 animals/group) and immunohistochemistry analysis was carried out to identify the number of astrocytes and GFAP fiber expression in the following hypothalamic nuclei: arcuate nucleus (ARC,
medium-ARCM and lateral-ARCL regions), PVN and lateral hypothalamus (LH).

**Results:** Control animals presented hypothalamic astrocytes mostly distributed around the vessels, with fine processes. In NIC animals, astrocytes were more distributed throughout the tissue, with higher immunoreactivity to GFAP, cellular hypertrophy, and processes of different astrocytes overlapping. The quantitative analysis of GFAP immunostaining showed an increase in its intensity in two nuclei of NIC animals, including the two different regions of the ARC: ARCM (which contains most of the NPY/AgRP cell bodies; +367%, p<0.05) and the ARCL (which contains most of the POMC/CART cell bodies; +178%, p<0.05); and in PVN (+210%, p<0.01). No difference was found in LH (p>0.05). The number of astrocytes was also higher in all nuclei analyzed of NIC animals: ARCM (+132%, p<0.05); ARCL (+110%, p<0.01); PVN (+144%, p<0.05); LH (+123%, p<0.05).

**Conclusions:** Our data indicates that programming by maternal exposure to nicotine during lactation leads to astrogliosis in different regions of hypothalamus in adult animals, which suggests inflammation, and it is probably due to obesity and hyperleptinemia of NIC animals.

Support: CAPES, FAPERJ, CNPq.