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ABSTRACT BOOK

SESSION 1 **POSTER 12**

EARLY POSTNATAL GENISTEIN ADMINISTRATION HAS A SEXUALLY DIMORPHIC OBESOGENIC EFFECT AND ORGANIZATIONAL EFFECTS ON HYPOTHALAMIC NEUROENDOCRINE CIRCUITS IN CD1 MICE

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Genistein (GEN), a phytoestrogen contained in soy and other legumes [1], may interfere with the endocrine system in multiple ways [2], including permanent morphological alterations of estrogen sensitive circuits in adult brain [3]. Several estrogen-sensitive systems are influencing food intake and energy expenditure (NPY, POMC, Orexin). Among them there is the Kisspeptin [4], originally identified as regulator of puberty and fertility. This system is a target for neuroendocrine disruption, in fact, exposure to EDCs altered the kisspeptin system in a region-,sex-and compound-specific manner, and induced effects on the timing of pubertal onset, estrous cycles, and socio-sexual behaviours [5].

We analysed the effects on adult CD1 mice of both sexes (age 2-months) of an early postnatal treatment (from PND1 to PND8) with GEN (50 mg/kg body weight dissolved in sesame oil) or with the vehicle (control, CON). We have immunohistochemically evidenced the expression of the anorexigenic POMC neuronal system within different hypothalamic nuclei [Paraventricular Nucleus (PVN), Arcuate Nucleus (ARC) and Dorsomedial Nucleus (DM)], of the Orexin system in the lateral hypothalamic area (LHA), and of the Kisspeptin system in the rostral periventricular area of the third ventricle (RP3V), PVN and ARC. In addition, we also tested different physiological parameters related to metabolism and reproductive system (fecal steroid hormones, mammary gland, gonads, uterus, vaginal opening).

Early postnatal exposure to GEN, in a dose comparable to the exposure level in babies fed with soy-based formulas, induced sexually dimorphic effects. GEN treatment induced

a significant increased body weight in adult GEN female (P<0,001), but there was no difference on food intake and daily feed efficiency. Moreover, still in GEN female we measured a significant decrease of plasmatic leptin (P<0,001) and T3 (P<0,05) concentration. POMC immunoreactivity was significantly reduced in adult GEN females compared to CON females only in PVN (FA, P<0,001), while we have not observed any significant difference in DM. We observed an increase of the positive cell number in the inner part of ARC only in GEN-treated females (P<0,01). The orexin system in the LHA is sexually dimorphic in CON mice (having males more cells than females), and this dimorphism was totally reverted in GEN mice: the cell number increased in GEN female (P<0,05) and decreased in GEN male (P<0,041). Kisspeptin immunoreactivity was significantly reduced in adult GEN females compared to CON females, whereas no changes were observed in males. Moreover, we measured many reproductive parameters. GEN treated males showed only a minor decrease of testicles' weight, probably related to the significant decrease of testosterone's concentration that we measured in feces (P<0,001). In females, GEN treatment induced an advanced pubertal onset (premature vaginal opening) and altered the development of reproductive system (increased urogenital distance and increased uterus' weight). In addition, GEN females showed an altered estrous cycle: in fact, the concentration of progesterone increased in the plasma (P<0,007) and the mammary gland present more tertiary branches (P<0,05).

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