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Giovanna Ponti

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THE SEXUALLY DIMORPHIC OBESOGENIC EFFECT OF EARLY POSTNATAL GENISTEIN ADMINISTRATION ON CD1 MICE

M. Marraudino[1,2], G. Ponti[1,3], A. Farinetti[1,2], S. Gotti[1,2], M. Keller [4], P. Collado[5], G.C. Panzica[1,2]

[1]Neuroscience Institute Cavalieri Ottolenghi (NICO), University of Turin, Turin, Italy; [2]Department of Neuroscience, University of Turin, Turin, Italy; [3]Department of Veterinary Sciences, University of Turin, Italy; [4]INRA, UMR 85 Physiologie de la Reproduction et des Comportements, Centre de recherche Val-de-Loire, Nouzilly, France; CNRS, UMR 7247, Nouzilly, France; Université François Rabelais de Tours, Tours, France; [5]Department of Psychobiology, Universidad Nacional de Educación a Distancia (UNED), Madrid, Spain.

Genistein (GEN), a phytoestrogen contained in soy and other legumes, may interfere with the endocrine system in multiple ways. In particular, GEN can act as 'obesogen' and increase the risk of developing metabolic disorders such as diabetes or obesity. The obesogenes increase body weight in mammals by acting on the fat tissue. Recent studies demonstrated that some of them (in particular the tributyltin) may induce permanent morphological alterations of estrogen sensitive circuits in adults as orexigenic and anorexigenic systems that influence food intake and energy expenditure. We analyzed 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). In particular, we examined the expression of the POMC neuronal system within different hypothalamic nuclei [Paraventricular Nucleus (PVN), Arcuate Nucleus (Arc) and Dorsomedial Nucleus (DM)] and the orexin system in the lateral hypothalamic area (LHA). 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. POMC immunoreactivity (measured as fractional area covered by the immunoreaction, FA) 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 and ARC, and in males. In addition, we observed an increase of the positive cell number in the inner part of Arc in GEN-treated females ($P<0,01$), whereas no changes were observed in males. 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 ($P<0,041$). In conclusion, the early postnatal exposure of CD1 mice to GEN determines long-term sex specific organizational effects on neural circuits controlling food intake and energy metabolism. The increase of weight on GEN female but not of food intake as well as the morphological alterations on the two circuits expressing orexin and POMC suggest that the effect on body weight is due to only alteration of metabolic regulation.