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**Early administration of the phytoestrogen genistein induces sex specific permanent alterations of nitric and vasopressinergic systems**

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Soy foods contain phytoestrogens as genistein (GEN) which may interfere with endocrine system and, during developmental critical periods, lead to permanent alterations of estrogen sensitive hypothalamic circuits. In a previous study, we demonstrated that GEN exposure through mothers resulted in an anxiolytic effect and a concurrent decrease of neuronal NO synthase (nNOS)+ cells in amygdala of male offspring [1]. This was consistent with both the role of NOS system in anxiety regulation and its sensitivity to gonadal hormones. In the present experiment, we analyzed anxiety levels and changes of neuronal circuits in mice directly fed with vehicle, Estradiol (E2) or GEN from birth (postnatal day 0, PND0) to PND8. Behavioral tests were conducted at PND60 and the mice were sacrificed at PND90. Coronal serial sections were processed for immunohistochemistry against nNOS and vasopressin (AVP). The GEN treatment had a dichotomic behavioral effects on sexes: anxiolytic on females while anxiogenic on males. Concurrently nNOS+ and AVP+ cell density in some hypothalamic nuclei was affected. Interestingly only a few of those effects were mimicked by E2 treatment suggesting that GEN may act through different intracellular pathways. These results raise concerns about the possible long-term effects of soy-based food in livestock that largely use soy-based supplements and show hypo-fertility problems, as pigs. Similar concerns could involve the long-term use of soy-based formulas for babies.

### References

- [1] Rodriguez-Gomez, Alicia, Federica Filice, Stefano Gotti, and GianCarlo Panzica. 2014. "Perinatal Exposure to Genistein Affects the Normal Development of Anxiety and Aggressive Behaviors and Nitric Oxide System in CD1 Male Mice." *Physiology & Behavior* 133: 107–14. doi:10.1016/j.physbeh.2014.05.020.

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### Keywords

Vasopressin; Nitric Oxide synthase; hypothalamus; anxiolytic; anxiogenic; sex differences; organizational effects.