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### **Chlorpyrifos hypothalamic alteration in developing mice**

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Exposure to endocrine disrupters can permanently influence the fetal programming of the endocrine system. The hypothalamus-hypophysis-gonad (HHG) axis is a complex system which influences the programming of several organs and their functions through feed-back mechanisms as well as different signalling proteins such as prolactin and oxytocin. Organophosphate insecticides (e.g. Chlorpyrifos, CPF) – still widely used in agriculture and against household pests - receive an increasing consideration for their possible interference with endocrine function, possibly by interacting with HHG axis. We present here preliminary data on the delayed effects of pre- and/or postnatal exposure to CPF on hypothalamic function of F1 female mice at dose levels devoid of maternal toxicity. Pregnant CD1 mice (10/group) were treated po with 0 (vehicle corn oil), 3, 6 mg/kg/bw/day of CPF on gestational days 15-18. Following delivery, 10 newborns/sex/group (F1) were treated subcutaneously on post-natal days (PND) 11-14 with: 0, 1, 3 mg/kg/bw/day of CPF.

Protein expression of prolactin and oxytocin were evaluated by western blot and ELISA analysis respectively, in the hypothalamus of F1 females sacrificed at adulthood (PND 150). Both protein levels were significantly higher in female mice that received only the prenatal treatment with 3 mg/kg/bw/day. Analysis of protein expression in F1 male mice are in progress. Our preliminary data suggest that prenatal exposure to CPF may up-regulate some major signalling proteins of HHG axis, with effects still evident at adulthood. The consequences of such altered endocrine programming deserve further investigation, also with respect to the reported changes in maternal and social behaviour of CPF-exposed females.

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