Si attesta che il Prof./Dr.

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SEXUALLY DIMORPHIC EFFECT OF CHRONIC TREATMENT WITH TRIBUTYLTIN IN THE ORGANIZATION OF BRAIN CIRCUITS INVOLVED IN THE *FOOD INTAKE* BEHAVIOR IN ADULT MICE

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Tributyltin (TBT), an antifouling agent of boat paints, is a common contaminant of marine and freshwater ecosystems. TBT is rapidly absorbed by organic materials and accumulated in fish, water birds, and mammals. Human exposure may be mediated by ingestion of contaminated food or by indirect exposure from household items containing organotin compounds. TBT is defined as an endocrine disruptor (EDCs) because it may bind to androgen receptors (ARs), it is also included in the list of obesogenic compounds. The brain is a target of TBT, as demonstrated by TBT acute administration inducing the expression of *C-fos* in the arcuate nucleus (ARC), a hypothalamic nucleus involved in the regulation of the *food intake*. Recent studies demonstrated that TBT interferes with the *food intake* system in mice, producing a strong decrease of circulating level of leptin and a reduction of NPY expression and its receptor (YR-1) in hypothalamic nuclei with sexually dimorphic effects. In this experiment we investigated the effect of a chronic treatment with TBT on the mouse anorexic system in both sexes. We investigated the POMC expression in PVN, DMH, VMH and ARC and the activation of leptin receptor, studying the leptin-induced P-STAT3 activation, in ARC. Our results show a sexually dimorphic effect of TBT on both systems studied: the TBT produced a significant decrease of POMC positive-structures in female mice in DMH, ARC and PVN, but not in male. Furthermore, in male mice, the TBT-treatment produced a decrease of PSTAT3 positive cells in ARC, while in female there is no effect on the number of activated leptin receptors. These results may help to better understand the obesogenic effect of TBT on the brain: it interferes with the anorexinergic system in hypothalamic areas involved in *food intake*, inhibiting the POMC expression in female but not in male mice. At the same time, this EDC affects the distribution of the activated leptin-receptors in ARC in male but not in female. In conclusion, the obesogenic effect of TBT is due to sexually differentiated effects on both orexigenic and anorexigenic systems, Y1 receptor, circulating leptin and its receptors.