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Zearalenon, an endocrine disruptor mycotoxin results in robust changes of gene expression in the uterus and in the hypothalamus.

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Zearalenone (ZEA) is a mycotoxin produced mainly by fungi belonging to the genus Fusarium in foods and feeds. It is frequently implicated in reproductive disorders of farm animals and occasionally in hyperestrogenic syndromes in humans. ZEA is a full agonist on estrogen receptor (ER) alpha and a mixed antagonist/agonist on ER beta and results in changes in transcription of estrogen sensitive genes that may have a potential to lead to adverse health hazards including reproductive and developmental effects. In our present experiments ZEA (0.1-10 mg/kg) was administered per os to immature female rats for 3 days (between PND 18- and 21). Positive controls were treated with 17-beta estradiol (E2) (0.04 mg/kg). Rats were decapitated, uteri and hypothalamic blocks were removed for histology and for measurement of mRNA expression in quantitative real time PCR. Immature rat uterotropic assay revealed that ZEA (5 and 10 mg/kg dose) resulted in significant increase in uterus weight without changes in body weight. ZEA administration increased the relative quantity of CALB3, C2 and SPP genes and decreased that of aquaporin5 and apelin mRNA levels in the uterus similar to that of E2. Within the hypothalamus, ZEA and E2 administration decreased the mRNA levels of urocortin2 (involved in metabolic and stress regulation) but had no effect on relative expression level of kisspeptin (that has been implicated in onset of puberty). Our results show that ZEA acts both centrally and peripherally and affects transcription of set of genes that may be implicated in the mediation of its' adverse effects on endocrine and neuroendocrine regulation.