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www.snf.ch
Wildhainweg 3, P.O. Box 8232, CH-3001 Berne

Division for Targeted Research
National Research Programmes
nfp@snf.ch

NRP Endocrine Disruptors

Final Summary

Original project title
Are organisational effects of estrogens on sexual differentiation, development and growth of fish mediated via the Insulin-like growth factor I (IGF-I) system?
Project leader
Prof. Manfred Reinecke, PhD
Project number
4050-66580

Interaction of (xeno)estrogens with the GH/IGF-I system in fish

Our aim was to verify our hypothesis that the organisational effects of estrogens on sexual differentiation, development and growth of fish are mediated via the Insulin-like growth factor I (IGF-I) system

Research questions

Hormones exert their effects in interaction with other autocrine, paracrine and endocrine factors. Our working hypothesis was that the action of (xeno)estrogens on fish sexual differentiation and growth is (partly) mediated via the insulin-like growth factor I (IGF-I) system that plays a central role in the regulation of growth, differentiation, and reproduction. The major source of circulating (endocrine) IGF-I is liver, but it occurs also in other organs where it likely acts locally (auto/paracrine). The main stimulants for IGF-I is growth hormone (GH) from the pituitary. As test substances, ethinylestradiol (EE2) and nonylphenol were chosen and as experimental species the tilapia – a fish species that is largely used in worldwide aquaculture. Since the estrogen-IGF-I interaction may occur at different hierarchic levels of IGF-I expression and be life stage-dependent, different developmental stages of crucial organs (brain, pituitary, liver, male and female gonads) are considered.

Results

In general, our hypothesis was verified: during fish development the local production of IGF-I in the organs investigated was disrupted by estrogens. The effects were obtained both by feeding of high doses of EE2 and by exposure to environmentally relevant concentrations of estrogens in the surrounding water. The developmental exposure to estrogens resulted in long-lasting impairing effects on the GH/IGF-I system. Because estrogens also reduced the expression of GH in the

pituitary, the effects seem to be exerted both indirectly at the level of pituitary (via inhibition of GH) and directly by suppression of local IGF-I in liver and extrahepatic sites, such as brain and gonads. Growth impairment caused by estrogens may be due to prolonged suppression of IGF-I synthesis in liver and its release leading to a lower concentration of circulating (endocrine) IGF-I.

Perspectives

Thus, estrogens and estrogenic compounds must be considered to have a higher impact as endocrine disruptors as yet thought because they interfere with a key hormonal system that is centrally involved in numerous processes of development, differentiation, growth and reproduction.