Differential Regulation of Aromatase Isoforms and Tissue Responses to Environmental Chemicals in Fish

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As in mammals, aromatase plays a basic role in fish reproduction. Unlike most mammals, with only one form of aromatase, fish have two distinct forms. One isoform, P450aromA, predominates in ovaries. Ovarian aromatase activity controls circulating levels of estrogens and is critical to female differentiation and development. Another isoform, P450aromB, prevails in brains and controls local aromatization of testosterone into estrogen, which is necessary for sex-specific reproductive behavior. The two isoforms derive from distinct genes that have unique regulatory 5'-flanking promoter regions, suggesting that a chemical signal could affect the transcription of the isoforms differently. The degradation times of mRNA for the two isoforms differ, with P450aromA degrading faster than P450aromB mRNA. In addition, differences in amino acid sequences between the isoforms relate to different levels of activity. Aromatase itself also has a number of phosphorylation sites that can regulate its activity and, because of differences in these sites, the two isoforms may have distinct sensitivities to phosphorylation. Because of the differences between isoforms in fish, we investigated whether chemicals that modulate aromatase activity might affect the two isoforms differently. Endocrine-disrupting chemicals (EDCs) have been shown to modulate aromatase activity. We compared the effects of four EDCs on reproduction and aromatase activity in brains and gonads from a marine fish, *Tautogolabrus adspersus*, treated *in vivo*. In spawning fish, testicular aromatase activity was low and not significantly affected by any EDC treatment. Estrogen treatment (estradiol or ethynylestradiol) significantly decreased aromatase activity in ovary and male brain, and resulted in lower egg production, viability and fertility. Treatment with octylphenol significantly increased only male brain aromatase activity, yet decreased egg viability and fertility. An aromatase inhibitor, androstatrienedione, significantly reduced male and female brain aromatase activity, as well as egg production and fertility, but had no effect on ovarian aromatase activity. Overall, our results demonstrate that different EDCs can affect the activity of brain and ovarian isoforms differently. Furthermore, changes in reproductive parameters were associated with alterations in the activity of either isoform. *This abstract does not necessarily reflect EPA policy.*