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Concern about the effects of Endocrine Disrupting Chemicals (EDCs) to fish reproductive health has stimulated the development and implementation of fish screening and testing procedures for EDCs which has become an important aim notably within the perspective of the EU regulatory framework for chemicals REACH (registration, evaluation, authorization and restriction of chemicals). Small fish species such as the zebrafish (*Danio rerio*) had appear as relevant models to identify EDCs, quantify their effects and explore their mode of action. In this context, transgenic zebrafish can provide suitable and practical biological models to study EDCs while reducing costs and the number of animals. For instance, we recently demonstrated the usefulness and relevance of a vivo mechanism-based test (the EASZY test that uses transgenic cyp19a1b-GFP zebrafish embryos) for rapid and cost-effective screening of estrogenic activity of chemicals. In the present work, our aim was to develop a panel of new transgenic models to study the expression and the perturbation of several target genes involved in the endocrine system and known to be affected by exposure to EDCs. These new transgenic zebrafish lines express Green Fluorescent Proteins (GFP) under the control of the zebrafish promoters of steroidogenic genes, i.e. cyp11c1 cyp19a1a. These genes are known to play a critical role in the biosynthesis of androgens and estrogens respectively and are affected by exposure to EDCs. The transgene is stably expressed across generations (>F3). Immunohistochemistry experiments showed that there is a perfect co-expression of GFP with endogenous zebrafish Cyp11c1 and Cyp19a1a proteins in the gonads. In both transgenic lines, GFP was localized in the cytoplasm of young oocytes and peri-follicular cells and in testes, GFP was localized in the cytoplasm of Leydig cells and germ cells. Since the fish brain is characterized by a strong ability to synthesize neuro-steroids, their expression in the central nervous system will be also considered.

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Effects of intracerebroventricular administered fluoxetine on cardioventilatory functions in rainbow trout (*Oncorhynchus mykiss*)

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Fluoxetine (FLX) is a selective serotonin (5-HT) reuptake inhibitor present in the aquatic environment which is known to bioconcentrate in the brains of exposed fish. FLX acts as a disruptor of various neuroendocrine functions in the brain, but nothing is known about the possible consequence of FLX exposure on the cardio-ventilatory system in fish. Here we undertook to investigate the central actions of FLX on ventilatory and cardiovascular function in unanesthetized rainbow trout (*Oncorhynchus mykiss*). Intracerebroventricular (ICV) injection of FLX (dosed between 5-25 µg) resulted in a significant elevation of total ventilation ($\dot{V}$TOT), with a maximum hyperventilation of +180 % (at a dose of 25 µg) compared with vehicle injected controls. This increase was due to an increase in ventilatory amplitude ($\dot{V}$AMP: +130 %) with minor effects on ventilatory frequency. The highest dose of FLX (25 µg) produced a significant increase in mean dorsal aortic blood pressure P_{DA}: +20 %) without effects on heart rate (fH). In comparison, intra-arterial injections of FLX (500-2500 µg) had no effect on ventilation but the highest doses increased both P_{DA} and fH. The ICV and IA cardio-ventilatory effects of FLX were very similar to those observed following injections of 5-HT, indicating that FLX probably acts via stimulating endogenous 5-HT activity through inhibition of 5-HT transporter(s). Our results demonstrate for the first time in fish that FLX administered within the brain exerts potent stimulatory effects on ventilation and blood pressure increase. The doses of FLX given to fish in our study are higher than the brain concentrations of FLX in fish that result from acute exposure to FLX through the water. Nonetheless, our results indicate possible disrupting action of long term exposure to FLX.

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