Developmental consequences of early life exposure to environmentally relevant concentrations of anti-depressive pharmaceuticals (fluoxetine) on behaviour and neuroendocrinology of fish

Pharmaceuticals are chemically stable molecules with highly potent effects on specific physiological targets which are usually evolutionary conserved across vertebrates. Human pharmaceuticals enter the aquatic environment through patient use and subsequent execration. Pharmaceuticals are often resistant to degradation and high concentrations have been reported in wastewater treatment effluents. Recipients of sewage treatment effluents are usually streams and shallow areas of lakes, environments which serve as spawning areas for many fishes. In the open waters of lakes and the sea, pharmaceuticals from sewage water effluents are diluted, resulting in low concentrations of these compounds[4]. Still, this type of contaminants has raised considerable concern. However, the fact that fish may be exposed to high concentrations of pharmaceuticals during early development may pose a much more serious threat to fish populations since some pharmaceuticals, especially antidepressants acting on the brain serotonergic system, have been reported to have life-long effects on behavior and physiology, effects that may even be transferred to the offspring through epigenetic mechanisms.

Fluoxetine is one of the most prescribed antidepressants and an environmental pollutant of concern found globally in aquatic environment[1–3]. Fluoxetine exerts its effects mainly through the inhibition of serotonergic transporter SERT, a protein which is highly evolutionarily conserved between zebrafish and mammals[5]. SERT clears the synapse of serotonin (5-hydroxytryptamine, 5-HT) by re-uptake of 5-HT to the pre-synaptic neuron. Thus, inhibition of SERT results in elevated synaptic 5-HT concentrations and an increase in serotonergic tone[6,7]. During early ontogeny 5-HT is critically involved brain development by acting on brain cell apoptosis, neuronal migration[9,10] and in the acquisition of “normal” anxiety-like and aggressive behaviour[8,11]. Early life exposure to fluoxetine could thus induce life-long effects on behaviour and neuroendocrinology, effects that could be transferred to offspring through epigenetic mechanisms.

The aim of this project is to determine whether (i) the exposure to environmental concentration of fluoxetine during early life stages results in altered monoamine transmission and behaviour of adult fish (developmental effect); (ii) the offspring of exposed fish will suffer the same behavioural and neuroendocrinological modulation (trans-generational, possibly epigenetic, effect).

Student project

For shorter projects students will take part in exposure of zebrafish embryos and behavioural testing of larvae (10 days post fertilization) and juvenile fish. The behavioural studies may also be combined with analysis of the brain serotonergic system.

For longer projects students will also take part in behavioural and neurochemical studies of adult fish and possibly also offspring of exposed fish.

Supervision

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