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Effects of mixtures of endocrine disrupting chemicals

Thyroid disruption and behavioural effects in fish models

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Abstract

Wildlife and humans are continuously exposed to thousands of man-made compounds, including chemicals that are able to act as endocrine disruptors (EDCs). These pollutants are able to affect vital processes including brain development, reproduction, metabolism and growth. An organism can be especially sensitive to these chemicals if the exposure occurs during early developmental stages, at so-called "windows of exposure" when organs that rely on endocrine regulation are still being developed. EDCs and other pollutants are present in the environment as complex mixtures, which can be difficult to handle from a risk assessment point of view. It is therefore important to evaluate effects of EDC mixtures after exposure during early development. The majority of the work in the current thesis was done by exposure studies using zebrafish. These studies take place within the EDC-MixRisk project, where an interdisciplinary whole mixture approach is used to assess effects of human-relevant EDC mixtures. This thesis is focused on three of the mixtures designed and produced within the EDC-MixRisk project, based on chemicals measured in serum of pregnant women and associated with adverse effects on neurodevelopment (MIX N0) or negatively associated with birth weight (MIX G0 and MIX G1) in their children.

Effects on behaviour and expression of genes related to the thyroid system were assessed in larval zebrafish after acute (48h) exposures using automatic locomotion tracking and qPCR. MIX N0, MIX G0 and MIX G1 were all found to significantly affect the locomotion of larval zebrafish at concentrations 100 times higher than the mean serum concentration measured in pregnant women (100X). Effects on thyroid receptor expression (*thra* and *thrb*) and deiodinases (*dio1* and *dio2*) were also observed for MIX N0 and MIX G1 at this concentration. For MIX G0, effects on gene expression (*thra*, *thrb* and *dio2*) were found already at 0.01X–1X concentrations (i.e. up to 100 times lower than the mean concentrations measured in women).

Next, we compared the two mixtures (MIX G0 and MIX G1) linked to adverse effect on growth by measuring locomotion over a longer period of time and found that the more complex MIX G1, which had the same total concentration as MIX G0 but consisted of more compounds, had an attenuated effect compared to MIX G0 immediately after exposure. However, when locomotion was measured one month later fish were still affected and moving less than compared to controls (hypoactive distance travelled) after MIX G1 exposure while MIX G0 no longer had an effect.

We also assessed the impact of environmental enrichment (EE) on exposure to the EDC mixtures. Our results showed that the rearing environment can affect the outcome of behavioural assays later in life for zebrafish acutely exposed to EDC mixtures. Additionally, adult fish reared in a barren or enriched environment and thereafter exposed to EDC mixtures can respond differently in a behaviour assay.

The final study included in this thesis was a field study of wild perch from sites in Sweden contaminated with known EDCs. We found that lifelong exposure to PFASs (one of the chemical classes present in the EDC mixtures described above) in a contaminated lake can affect both the thyroid system and immune defence in wild perch.

Keywords: Endocrine disrupting chemicals, ecotoxicology, zebrafish, perch, locomotion, behaviour, thyroid disruption, EDC mixtures