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Environmental, Nutritional and Endocrine Regulation of Metabolic Processes in Fish

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ABSTRACT

Due to seasonal variations in temperature and food availability, fish in temperate regions should be able to make metabolic adjustments to ensure that enough energy is available for the maintenance of basal processes. The major aim of this thesis was to elucidate how the physiology and lipid metabolism of salmonid fish is affected by temperature and food availability, and to clarify aspects of the endocrine control of lipid metabolism.

In this thesis, the effects of increased temperature or reduced food availability were studied in salmonids by employing a non-prejudiced metabolomics approach to assess the physiological responses. Detailed information on the abundance of specific amino acids, lipid classes, fatty acids and other metabolites in tissue extracts and plasma was obtained by nuclear magnetic resonance (NMR) based metabolomics. NMR-based metabolomics were successfully employed and proved to be applicable to studying metabolic fluxes in fish, providing data on novel and integrated responses. The results show similar changes in lipid metabolism during food deprivation and elevated temperature. The observed responses included increased plasma very-low-density lipoprotein (VLDL) and unsaturated fatty acids (FAs) concurrent with decreased high-density lipoprotein (HDL) and choline. The changes during starvation also involved changes in amino acids and glycogen that indicate that amino acids are used for gluconeogenesis in the liver to preserve glycogen stores.

Growth hormone (GH) has both lipolytic and lipogenic effects. To further elucidate the mechanisms of GH action on salmonid lipid metabolism, the effects of GH *in vivo* on the transcription of several key lipid metabolism enzymes in various tissues were investigated. GH inhibited the hepatic expression of lipoprotein lipase (LPL) thereby decreasing hepatic lipid uptake. Hormone-sensitive lipase (HSL) mRNA expression was not increased by GH in any of the studied tissues, suggesting that the well-known GH-induced lipolysis is regulated on posttranslational levels in rainbow trout. The regulation lipid metabolism in salmonids was further investigated by studying direct effects of FAs and ghrelin on freshly isolated cells from mesenteric adipose tissue and liver. FAs elicited acute negative effects on lipid storage by decreasing lipid uptake via LPL activity in adipose cells as well as by stimulating lipolysis of stored triglycerides (TG) in liver cells.

Together the results presented in this thesis shows that elevated, suboptimal temperature and nutritional may have propound effects on important processes as growth, food intake and the metabolome of salmonid fish, and may lead to a negative energy balance. Metabolic changes may be mediated by hormonal and nutrient factors acting at gene expression or enzyme activity level. The results may contribute to better understand lipid deposition patterns in farmed fish and potential effects of climate change on salmonids in the wild and in aquaculture.

KEYWORDS: lipids, metabolism, temperature, fasting, growth hormone, ghrelin, NMR, metabolomics, *Salmo salar*, *Oncorhynchus mykiss*

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