(porphyrin accumulation) compared with their wild type counterparts. L*Fxr*KO mice mimicked diminished ductular reaction, while I*Fxr*KO mice exhibited severe ductular reaction similar to that of wild type mice, indicating that the ductular reaction is dependent on hepatic FXR. ChIP-Seq for FXR revealed binding peaks in the heme biosynthesis genes, *Alas1*, *Alad*, *Uros*, and *Fech*, suggesting that FXR may act as a transcription factor for these genes. Further investigation revealed that *Pbgd* gene expression was increased, while *Fech* gene expression was decreased in female FxrKO mice compared to wild type mice. In male mice, *Pbgd*, *Uros*, *Urod*, and *Cpox* gene expression was increased in the absence of *Fxr*. In conclusion, *Fxr* is necessary to mount a ductular reaction and plays a key role in heme biosynthesis in the liver.

Steroid Hormones and Receptors

STEROID HORMONES, NUCLEAR RECEPTORS, AND COLLABORATORS

Maternal Total Cortisol Levels in Early Pregnancy Depends on Fetal Sexual Dimorphism. But Finally No Association With Birth Weight

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Enhanced maternal cortisol levels may have a negative impact on fetal development with a higher risk for diseases later in life, e.g. premature cardiovascular disease and type 2 diabetes. Prior studies do assume even a sex specific impact. Currently, it is unknown whether sexual dimorphism in the fetus could display a different maternal cortisol level that is associated with intra uterine growth. In the present study (performed in the Amsterdam Born Children and their Development (ABCD) –cohort), we evaluated in 3049 pregnant women (in early pregnancy) whether fetal sex is related to the level of maternal serum total cortisol and whether this contributes to fetal growth. Maternal serum total cortisol levels increased along early pregnancy from on average 390±22 nmol/L (at 5th week of pregnancy) to 589±15 nmol/L (at 20th week of pregnancy). The presence of a female fetus was associated with higher maternal total cortisol level in a distinctive time interval along early pregnancy; before 11th week of pregnancy, no difference, and from the 12th week of pregnancy a difference of 15 (SE:7) nmol/L between mothers carrying a male vs female fetus was found and that difference increased to 45 (22) nmol/L at 20th week of pregnancy (p-for-interaction=0.05). Maternal serum total cortisol levels were negatively associated with maternal age, pBMI, smoking and parity, the last one also increasing with pregnancy duration. After adjusting for these factors, the association between fetal sex and maternal cortisol remained Maternal serum total cortisol levels were significantly associated with birth weight, standardized for pregnancy duration (ß -.22; SE:0.06; P < 0.001). Girls had a significantly lower birth weight (-132 SE:16 gram) compared to males, however, maternal cortisol did not alter the association between fetal sex and birth weight to a relevant degree indicating no mediation by maternal cortisol. In early pregnancy, the maternal total cortisol levels are related to fetal sex. However this difference in maternal total cortisol level was finally not related to birth weight.

Steroid Hormones and Receptors

STEROID HORMONES, NUCLEAR RECEPTORS, AND COLLABORATORS

Measurement of Steroid Fatty Acyl Esters in Blood and Brain

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Steroid fatty acyl esters (FAEs) are a class of steroid conjugates that are abundant in circulation, have long half-lives, and are stored in lipid-rich tissues. Steroid-FAEs are present in many species, but their functions are poorly understood. They can be metabolized to active, unconjugated steroids and therefore may act as a reservoir of steroids. Dehydroepiandrosterone (DHEA) is an androgen precursor that can be conjugated to various fatty acids. DHEA also modulates aggression in several species, including songbirds, rodents and humans. Recent studies suggest that DHEA-FAEs might be present in songbird blood and/or brain, in part, to regulate aggression. Here, we (1) investigated the abundance of multiple fatty acids in songbird blood and (2) developed an indirect method to measure DHEA-FAEs in songbird blood and brain. First, preliminary work demonstrated high circulating levels of total (esterified and non-esterified) fatty acids, especially oleic, linoleic, and palmitic acids. These data, in conjunction with previous research, suggest that these fatty acids might be conjugated to steroids, including DHEA. Second, we successfully developed a saponification technique to indirectly measure DHEA-FAEs. Saponification cleaves the bond between the steroid molecule and the fatty acid, and we then measure the unconjugated steroid. DHEA-FAEs were incubated in 0.5M potassium hydroxide in ethanol for 30 min at room temperature, and steroids were subsequently extracted twice with dichloromethane. Unconjugated DHEA was quantified using liquid chromatography-tandem mass spectrometry (LC-MS/MS), the gold standard in steroid measurement. DHEA recovery was 88% using reference standards in neat solution. We validated this method with song sparrow plasma and chicken serum and obtained recoveries of 94-105% with intra-assay variation of 2.6%. Future research will directly measure specific DHEA-FAEs (e.g. DHEA-oleate) in blood and brain using LC-MS/MS. This research will elucidate the possible roles of steroid-FAEs in brain function and the regulation of steroid-dependent behavior. This work may also clarify the identities, levels and functions of steroid-FAEs in other species, including rodent models and humans. These data have implications for basic and clinical neuroendocrinology, offering insights into a possible storage system for steroids that may influence social behaviour.