Summary

Placental hypoxia is commonly considered to play an important role in the development of several perinatal and neonatal diseases such as intrauterine growth retardation (IUGR) or preeclampsia. In this disertation we therefore tried to (at least partially) solve this problem by answering the question how do acute and chronic hypoxia affect fetoplacentar vasculature.

Unlike all vascular beds with the exception of the pulmonary circulation, fetoplacental vessels respond to acute hypoxia with vasoconstriction (HFPV). This mechanism presumably diverts blood flow from poorly oxygenated areas towards regions with better O2 supply. We already know, that hypoxia inhibits potassium channels and thus causes depolarization in fetoplacental vascular smooth muscle. We propose that this hypoxia-induced depolarization leads to vasoconstriction by activating voltage-dependent calcium (Ca) channels and Ca
influx.

We performed our first experiment on the preparation of dually perfused cotyledon of the human placenta, which we gained immediately after uncomplicated spontaneus deliveries or elective caesarian sections. The preparation was perfused with Krebs´ saline with dextran and meclophenamate and gased with 40% O_2, 5% CO_2 a 55% N_2.

We compared HFPV, which was elicited by changing gasing of the perfusate to the mixture with 0% O2+5%CO2+95%N2, between isolated perfused human cotyledons treated with an inhibitor of L-type channels, nifedipine, and preparations receiving only vehicle. While the solvent (diluted DMSO) had no inhibitory effect on HFPV, the hypoxic responses were completely abolished,
even by a relatively low dose of nifedipine (1 nM). We conclude that activation of L-type Ca channels is an essential part of HFPV.

However, for the development of the diseases mentioned above, chronic rather than acute hypoxia is likely to play a role, and the effects of chronic hypoxia on the placental vascular bed is not well known.

The aim of the second study was to evaluate the influence of chronic hypoxia on the fetoplacental vascular resistance and reactivity to vasoconstrictor stimuli. Because it would be ethically impossible to use the same preparation as in the previous experiment for this research, we had to use an animal model-dually perfused rat placenta.

We exposed rats to normobaric hypoxia (10% O2) during the last week of the 3-week pregnancy. One day before the expected date of delivery, they were anesthetized. One placenta was dually perfused (from both the maternal and fetal side) with Krebs' saline and gased with 21%O2+5%CO2+74%N2. To characterize fetoplacental resistive properties, the pressure-flow relationship (P/Q) was evaluated by measuring perfusion pressure while increasing flow rate in 0.2 ml/min steps. To asses vascular reactivity we administred three increasing doses of angiotensin II to the fetal circuit and then perfomed two hypoxic challenges (gassing the perfusate with 0% O2+5%CO2+95%N2). The P/Q lines were significantly shifted towards higher pressures in the hypoxic rats but unaltered by a high dose of a vasodilator, sodium nitroprusside, in either group. The reactivity to angiotensin II was increased in placentas from hypoxic rats as compared to normoxic controls. The vasoconstrictor responses to acute hypoxic challenges were also higher in hypoxic rats. We conclude that chronic hypoxia causes elevation of fetoplacental vascular resistence refractory to vasodilators and increases fetoplacental vasoconstrictor reactivity both to angiotensin II and acute hypoxic challenges.