Fetal-neonatal induced hypo- and hyperthyroidism affects Leydig and Sertoli cell development.

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Fetal-neonatal induced hypo- and hyperthyroidism affects Leydig and Sertoli cell development

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Previously the effects of neonatal induced hypo- and hyperthyroidism have been investigated in rats using rather unphysiological approaches like propyl-thiouracil (PTU) treatment or daily injections with high doses of triiodothyronine (T3). A disadvantage of PTU is that it also has a direct effect on Leydig cell function and PTU can not be administered during pregnancy due to the occurrence of spontaneous abortions. The downside of using T3 is that the half-life is short, and the high doses used over the years induces far more unpleasant side effects than wanted.

In the present line of research mild forms of hyper- and hypothyroidism are induced already during fetal development. Dams of the hypothyroid groups are fed an iodine-free diet to which perchlorate is added two weeks prior to mating to deplete endogenous iodine stores. Dams and offspring were kept on the diet until sacrificed. To induce hyperthyroidism the iodine-free diet was supplemented with iodine and thyroxin.

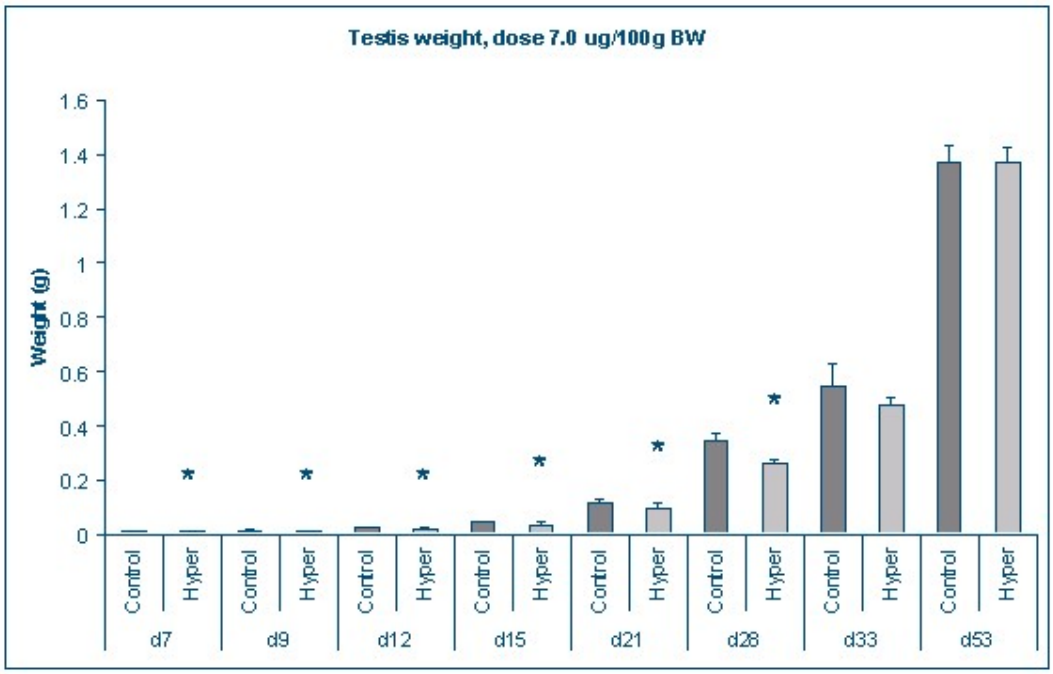
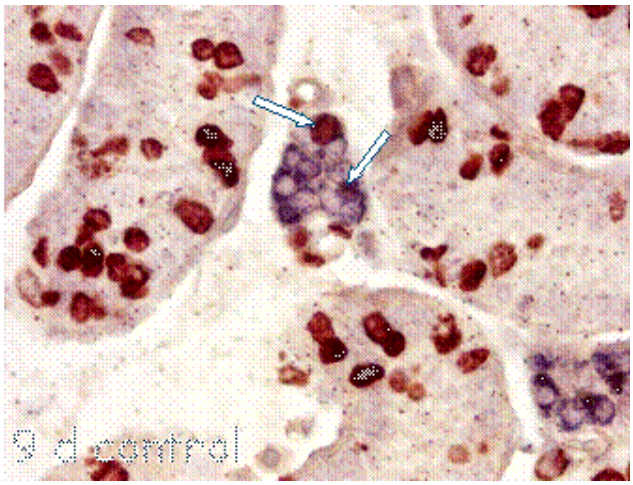


Figure 1. Testis weight of hyperthyroid animals.

Both hyper- and hypothyroidism result in a decrease in body and testis weight of the pups. The primary focus on organ and tissue level is on the brain and on the gonads. Last years we found some interesting effects of hyperthyroidism on anatomical brain development. Nowadays we are doing some behaviour experiments to clarify the effects of the treatments for behaviour and learning processes.

The gonads are still a focus of our research. In contrast to the controls, testis development is significantly delayed in the testes of hyperthyroid pups, where Leydig cell proliferation is enhanced. Adult-type Leydig cell (blue cells in Figure 2) proliferation, as identified by bromodeoxy-uridine (BrdU) incorporation (the brown cells in Figure 2) and 3ß-hydroxysteriod dehydrogenase (3ß-HSD) labelling (this gives the blue colour to the Leydig cells), was slightly lower in the hyperthyroid animals up to day 15, but significantly increased above control levels from day 21 onwards (Figure 3).



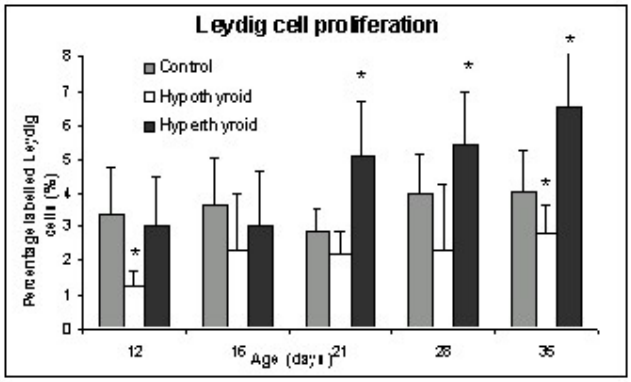


Figure 2+3. 3ß-HSD labelling of Leydig cells and Leydig cell proliferation in hypo- and hyperthyroid rat pups

Sertoli cell development can me measured by tubular lumen formation in the testis. Therefore we look for opening of the lumen of the tubules of the testis (Figure 4). What you can see in this figure is the opening of the tubules of the testis when the animals grow older. The hypothyroid animals show later opening.

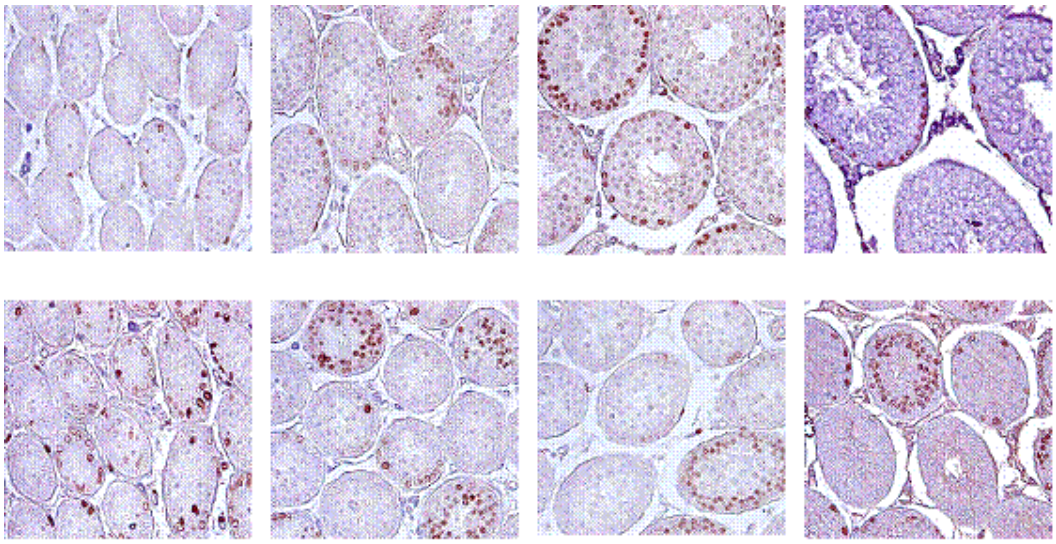


Figure 4. Tubular lumen formation in hypothyroid rat pups.

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