6. Summary

Examinations on anxiety behaviour of transgenetic rat TGR (mRen2)27

Although for over the last 30 years anxiety and anxiety diseases have been object of extensive research, not much is known about the mechanisms which regulate emotional processes and which mechanisms are responsible for the changes in the brain during anxiety diseases. Examinations on gene manipulated laboratory animals can provide new insight into the mechanisms of anxiety and anxiety disease.

The transgenic rat TGR(mRen2)27, which was developed from Hannover-Sprague-Dawley-rats, has an additional renin gene. Due to this the blood pressure of the rats is increased.

This study focuses on the anxiety behaviour of the transgenic animals in comparison to the Sprague-Dawley-rats. To date the behavioural pattern of the Sprague-Dawley-rats has not been compared in any detail to that of other rat strains. Therefore the second part of this thesis compared the behavioural patterns of various rat strains and of Wistar-rats originating from different breeders.

The effects of the additional renin gene on the physiological body functions was investigated by monitoring the feeding and drinking behaviour and the development of the body weight of the transgenic animals in comparison to the negative control rats. The amount of drinking water consumed was increased in the transgenic animals. This result confirmes that there is a direct correlation between high blood pressure and the renin-angiotensin-aldosteron-system.

The anxiety behaviour was examined in the white- and black open-field-test, in conflict-test, social-interactions-test, the holeboard-test, a black-white-box-test, an elevated-plus-maze-test and a free-exploratory-paradigm-test. The anxiolytic effects of diazepam (1 and 3 mg/kg) and propranolol (1 and 3 kg/mg) were studied in the elevated-plus-maze-test.
In summary, there were no marked differences in behaviour between the TGR(mRen2)27and the wildtype. Some behavioural changes could be seen repeatedly on several occasions, but could not always be statistically verified.

The TGR(mRen2)27 showed less locomotor activity. This parameter does not correlate directly to increased anxiety behaviour, but it cannot be considered as independent.
Interestingly, in our study, as well as in the literature the TGR(mRen2)27 overcame their fear faster than the Sprague-Dawley-rats after stimuli like food and water deprivation. Both diazepam and propanolol showed an anxiolytic effect on the transgenic mice, but not on the Sprague-Dawley-rats.

Differences in anxiety behaviour were examined between the rat strains Sprague-Dawley-, Wistar-, Lewis-, Fischer- and Brown-Norway- and between Wistar-rats of three different breeders. Therefore the locomotory activity was examined in the open-field-test and the anxiety-related behaviour in a conflict-test, a social-interaction-test, a holeboard-test and a free-exploratory-paradigm-test. The results show that robust behavioural differences exist between different strains of rat and even animals of one strain, obtained from different breeders.
Accordingly it is necessary to carefully select appropriate rats for behavioural studies. In conclusion, national and international comparisons of results are only possible on one kind of rat strain. Different rat strains can have different „levels of anxiety“ therefore depending on the anxiety level of the rat different responses can be induced and the effects of drugs cannot be registered.

Based on the result that Sprague-Dawley-rats did not respond to the treatment with anxiolytics in the elevated-plus-maze-test and showed a lower anxiety behavioural profile in three of four behavioural tests the question arises, whether the above described anxiety tests are qualified to register behavioural changes in this rat strain.