

## 7 Summary

Hitherto the term for addiction in studies on animals was normally used to describe the observation of a preference development. It was not until the beginning of the nineties that various authors started to lay down further criteria for the study of behavioural dependence. WOLFFGRAMM and HEYNE (1995) described for the first time an animal model for the induction of behavioural dependence of rats to various addictive drugs. This was examined against the criteria that had been laid down by them. Within studies of MÜLLER (2001) and PIRK (2002) it was not possible to reproduce these findings. That is why in this study – after further modifications had been made to the animal model described – an attempt was made to induct behavioural dependence on alcohol and the  $\mu$ -opiate agonist etonitazene in male and female Wistar rats.

The alcohol was presented to the animals in the framework of a “free-choice-model”, either at regular intermittent intervals (48 hour rhythm) with an initial high dose (20%), or at irregular intermittent intervals with changing concentrations or in regular increased alcohol concentrations. After about 30-46 weeks of exposition to alcohol the development of behavioural dependence was examined against the criteria of WOLFFGRAMM and HEYNE. The etonitazene solution (2,0 $\mu$ g/ml) was presented similarly to the rats as in the experiments with the alcohol in the framework of a “free-choice-model”, either at regular intermittent intervals (48 hour rhythm), or as continuous availability. In a further experiment the etonitazene solution was readily available by forced presentation in increased concentrations (in approximately 31 weeks an increase from 0,2 $\mu$ g/ml to 2,0 $\mu$ g/ml). Depending on the experiment after 17 to 48 weeks of exposition to etonitazene an examination of the behavioural dependence was carried out against the criteria of WOLFFGRAMM and HEYNE. In the experiments with alcohol the rats actually developed a preference for it (especially during the regular intermittent doses of initially 20% a massive increase in consumption of up to 24,31ml/kg bodyweight/d was induced), however, with the additional offer of saccharose-water all of the animals reduced their alcohol consumption considerably. None of the rats proved to have developed behavioural dependence. In the course of the experiments with etonitazene an increase in consumption could not be established even after many weeks of exposition. The animals did not develop any behavioural dependence on etonitazene but rather an apparent aversion to the drug.

To summarize it was established that even after further modification of the animal model according to WOLFFGRAMM and HEYNE (1995) and in the framework of this study,

neither behavioural dependence on alcohol or on the  $\mu$ -opiate agonist etonitazene could be induced. Therefore this study confirms the results of the experiments carried out by MÜLLER (2001) as well as those of PIRK (2002).