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Dissertations-Kurzfassung

Development of Reward Sensitivity and its Association with the Endocannabinoid System

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The present doctoral thesis aimed to systematically study the development of reward sensitivity during the course of life in the rat with a specific focus on puberty and aging. In the course of life the brain is subjected to maturational and degenerative processes which alter and effect the regulation and functioning of multiple cognitive and affective processes. Specifically, the function of the cortico – basal ganglia reward circuitry seems to underlie age-related alterations during adolescence and aging which might give rise to altered reward processing and sensitivity for reward characteristics.

Epidemiological studies indicate an increased vulnerability to the initiation of drug use and abuse during adolescence. Interestingly, human studies indicate a hyperactivity of striatal reward-associated structures in adolescence which might be linked to enhanced sensitivity towards rewards. The first study of the present thesis characterized the development of reward sensitivity towards a natural food reward in the whole timecourse of adolescence in male rats (postnatal days (pd) 30-90) by monitoring consummatory and motivational behavior, as well as neurobiological correlates of reward. The repeated measurement of limited-access intake of sweetened condensed milk (SCM) revealed transiently enhanced consumptional levels during puberty (pd40-60) which were specifically pronounced around mid-puberty (pd50). In parallel, the motivational incentive properties of SCM and the c-fos protein expression in reward-associated brain structures in response to a SCM-conditioned odor cue were significantly higher in pubertal than adult rats and similarly peaked at mid-puberty. These data indicate an increase in reward sensitivity during adolescence accompanied by enhanced responsiveness of reward associated brain structures to incentive stimuli, which appear to be strongly pronounced around mid-puberty.

In order to investigate the sensitivity for drug rewards during puberty a second study assessed the acute, chronic and lasting effects of pubertal and adult cannabinoid treatment on repeated alcohol intake and on alcohol reward in male rats by using 5% alcoholic beer and 5% ethanol solution. Acute administration of the synthetic cannabinoid agonist WIN 55,212 (WIN) exclusively stimulated initial alcohol intake in pubertal rats, whereas no effects were observed in adult rats. A subsequent chronic WIN treatment stimulated alcohol intake in pubertal and adult rats, but was more pronounced for the pubertal treatment. The effects observed were similar for both alcoholic solutions. After an abstinence phase, the lasting effects of pubertal and adult WIN treatment on consumptional and motivational aspects of alcohol were evaluated in adult rats. Whereas adult-treated rats showed no lasting WIN effects, pubertal cannabinoid treatment promoted consumption and the reinforcing effects of ethanol in adulthood. Additionally, alcohol exposure during puberty was found to increase adult sensitivity for alcohol reward, which was most prominent for beer. These data provide clear evidence for enhanced vulnerability towards the rewarding effects of natural incentives and drugs during puberty which might promote the initiation and continuation of drug use in adolescents. Additionally, pubertal but not adult drug consumption had lasting effects on later drug intake and responsiveness which might be associated with higher risk to develop severe addictive disorders and drug abuse problems in later life.

The third study investigated the development of reward sensitivity during the aging process for a natural reward in rats. Repeated intake of SCM in limited-access tests revealed a progressive decline of consummatory behavior during the course of aging. The properties of hedonic, motivational and consumptional aspects of SCM were further characterized in senescent rats (22 month) and compared to adult controls. Aged animals consistently showed decreased reward sensitivity as measured with pleasure-attenuated startle, conditioned place preference, progressive ratio and limited-access SCM consumption. This age-related decline in reward sensitivity might be related to neurodegenerative aging processes which affect the cortico – basal ganglia reward system and potentially underlies the development of depressive symptoms which show a high prevalence rate in elderly humans.

Perception of pleasure and rewards is important for human well-being and mental health. The regulation of reward sensitivity might be critical for the development of mental disorders and therefore, the developmental changes in reward sensitivity should be considered more thoroughly in etiological models and in prevention as well as in intervention programs of public health care.