

## Ruprecht-Karls-Universität Heidelberg Medizinische Fakultät Mannheim Dissertations-Kurzfassung

## From adolescence to adulthood: characterizing the enduring consequences of adolescent adversities in rats

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This thesis investigates the prolonged effects of various adolescent adversities on behavior and neurobiology in male and female rats. We employed a reverse translational approach. This method applies insights from human studies to animal models, enhancing our understanding of underlying human phenomena. The thesis focuses on the long-term behavioral consequences of adolescent social isolation (ASI), social instability stress (SIS), and peer rejection (PR), highlighting, adversity, timing and sex differences. Notably, we placed a special emphasis on exploring the oxytocin (OT) system, but only in the context of ASI.

The initial study explored how ASI timing (early or late) affects adult social and anxiety-like behavior, alongside OT receptor (OTR) binding in key brain regions. Early ASI notably increased OTR binding in the paraventricular nucleus (PVN) and thalamus (PVT) in female rats, impacting various behaviors, particularly social recognition memory and thermal pain sensitivity. We manipulated OT release from the PVN into the PVT and found that endogenous OT release had non-specific treatment effects on social recognition memory.

Subsequent studies examined social instability stress and its immediate and long-lasting behavioral impacts. SIS exposure led to reduced anxiety-like behavior and social interactions, regardless of sex or age, but enhanced social recognition memory in both sexes. Interestingly, male rats displayed a greater preference for new social contacts over familiar ones, indicating a unique behavioral profile characterized by reduced anxiety and altered social behavior. Thus, SIS in Wistar rats may represent environmental enrichment rather than a stressor.

The final study utilized a novel adolescent peer rejection model to analyze its long-term effects on alcohol-seeking behaviors, locomotion, and sucrose preference in both sexes. Notably, peer-rejected females exhibited increased susceptibility to alcohol cues, while males showed resilience, unaffected by changes in locomotion or sucrose reward sensitivity. This sex-dependent response suggests that peer-rejected female rats are a critical model for studying relapse-like behaviors akin to clinical observations.

In conclusion, this thesis describes the intricate and enduring behavioral impact of adolescent adversities (ASI, SIS, PR) on social and anxiety-like behaviors, highlighting notable adversity, timing and sex differences. The findings, particularly in female ASI rats, underscore potential therapeutic avenues within the OT system and offer insights into the developmental trajectory post-ASI. The reverse translational approach, integrating behavioral and molecular methods from humans to rats provides us with an approach that can improve translation in the future.