



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

**Pathways contributing to the Risk of Substance Use Disorders after
Adverse Childhood Experiences**

Autor: Sarah Viviane Gerhardt
Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)
Doktormutter: Prof. Dr. S. Vollstädt-Klein

Substance use disorders are a major global health problem. Worldwide, over 35 million individuals suffer from substance use disorders, adding to 283 million individuals who are affected by alcohol use disorder. Being both a risk factor and consequence of substance use, alterations in the structure and function of the brain take place, for example, in regions relevant for reward, stress, and emotion processing. However, merely considering neurobiological aspects does not do justice to the complexity of the disorder. Previous research suggests that adverse childhood experiences, for instance, childhood maltreatment (i.e., emotional, physical, and sexual abuse, as well as emotional and physical neglect), are an important risk factor in the etiopathology of substance use disorders.

As such, these experiences also affect the neurobiology of an individual, which might just as well lead to alterations in reward, stress, and emotion processing – and, thus, result in an earlier onset of substance use disorders or hamper treatment success. In this context, substance craving and impaired emotion processing are of importance as they may facilitate relapse, which, in turn, maintains a substance use disorder.

This dissertation, therefore, integrates neurobiological and societal aspects to address pathways contributing to the risk of substance use disorders. To this end, an individual's history of childhood maltreatment – one major aspect of adverse childhood experience – will be explored in depth.

Study 1 examined 655 treatment-seeking individuals with substance use disorders and revealed high prevalence and severity of all subtypes of childhood maltreatment. In this sample, women and individuals with cannabis use disorder were most severely affected, especially by emotional abuse. Emotional abuse, but not other subtypes of childhood maltreatment, positively related to substance craving at admission to treatment. However, symptoms of depressiveness, anxiety, and perceived stress influenced craving severity at admission and craving reduction during treatment rather than childhood maltreatment severity. The results revealed a subtype-specific influence of childhood maltreatment, and, furthermore, demonstrated the significance of type of substance and sex/gender. This study illustrated the importance of including the aspect of childhood maltreatment in individualized treatment approaches.

Study 2 addressed neural correlates of emotion processing and expanded previous findings of altered amygdala functioning in individuals with alcohol use disorder by applying a habituation index. Further, the relation between amygdala habituation to repeated aversive emotional stimuli and childhood maltreatment was examined. Individuals with alcohol use disorder exhibited not only deficient amygdala habituation, compared to healthy individuals. Beyond that, the temporal pattern of habituation resembled neural sensitization, thus, showing a unique amygdala habituation pattern compared to other mental disorders such as post-traumatic stress disorder. While no relation between childhood maltreatment and amygdala habituation was observed for individuals with alcohol use disorder, healthy individuals exhibited increase habituation in relation to more severe physical and emotional neglect. Lastly, a significant relation between higher alcohol intake and reduced amygdala habituation was observed to be independent of the clinical status of the participants, which might indicate short-term substance effects. The study revealed, thus, novel evidence regarding alterations in emotion processing in alcohol use disorder that might open a new avenue for treatment targets.

Taken together, the two studies demonstrated the relevance of addressing adverse childhood experiences, and informed about pathways leading to substance use disorders. Integrating this societal aspect into neurobiological research reveals new opportunities for treatment strategies.