



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

**The association between adverse childhood experiences and  
alcohol use disorder: probing risk and protective factors**

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

While existing studies have established an association between adverse childhood experiences (ACE) and the development of alcohol use disorder (AUD), there is a paucity of research on potential mechanisms underlying this association and on factors that might moderate it. The aim of this dissertation was to address these gaps, focusing on both risk and protective factors.

Study I assessed the association between ACE and changes in brain structure in adults with AUD, compared to a healthy control group (N = 63). The role of the type and timing of ACE was explored using a machine learning approach. Adults with AUD showed significantly reduced cortical thickness in brain regions linked to inhibitory control, notably in the left inferior frontal gyrus, compared to healthy controls. This reduction in cortical thickness was associated with higher ACE severity, specifically higher levels of abuse experienced during early adolescence, suggesting the potential relevance of inhibitory control in the association between ACE and AUD.

Study II extended Study I by examining the association between ACE and inhibitory control in heavy-drinking adults (N = 32) using a functional MRI-based behavioral inhibition paradigm (stop-signal task). Interestingly, greater ACE severity was associated with better inhibitory control in this population, which appeared to be driven primarily by emotional neglect. Lower activation in the left inferior frontal gyrus during successful behavioral inhibition, which was associated with higher levels of emotional neglect, may potentially reflect increased neural efficiency of inhibitory control after more severe emotional neglect, warranting further investigation in longitudinal studies.

Study III was a longitudinal study (N = 3422) that assessed adolescent alcohol use trajectories in relation to family-specific negative life events, sports participation, and their interaction. There was a negative effect of negative life events on initial alcohol use such that each additional event was associated with greater alcohol use in early adolescence. Alcohol use was initially lower for youth with a higher number of negative life events (three or more) who engaged in sports more frequently (24 days per month), but increased precipitously over time such that it was similar to those without negative life events by the final assessment. High sports participation delayed the onset of risky alcohol use and reduced alcohol use in adolescents with a high negative life event load primarily during early adolescence.

Study IV was a systematic review and preliminary meta-analysis of six controlled intervention studies (N = 327) examining whether a time-efficient form of exercise, namely high-intensity interval training, can improve health outcomes in patients with substance use disorders. Preliminary results suggested that high-intensity interval training may improve cardiorespiratory fitness ( $VO_{2max}$ ) and reduce substance craving in this population, potentially improving treatment outcomes and lowering the risk of relapse.

A key finding from Studies I and III is that early adolescence (years 13-15) appears to be a sensitive developmental period for both increased alcohol use and neural changes related to early life adversities. Study I additionally highlighted the importance of the type of adversity, as changes in brain structure were related specifically to abuse – but not neglect – during this developmental period. During the same period, increased sports participation emerged as a protective factor for mitigating the effects of negative life events on alcohol use. This protective effect, however, was dose-dependent such that benefits were observed only in adolescents who experienced multiple negative life events and engaged more frequently in sports. Studies I and II further emphasized the importance of inhibitory control in the relationship between early life adversities and alcohol use disorder. However, this relationship may be more complex in nature and potentially contingent on the ACE subtype and developmental stage. Study IV reviewed evidence suggesting that physical exercise may positively impact inhibitory control in individuals with substance use disorders through improved cardiorespiratory fitness, though the role of exercise intensity requires further investigation.

Collectively, these findings highlight 1) the potential of physical exercise and sports in prevention and intervention programs, 2) early adolescence as a potential “window of opportunity” for such programs, and 3) the need for further longitudinal research to explore the role of different types of ACE, cognitive functioning (in particular inhibitory control) and neurobiological changes over time using neuroimaging techniques.