Ruprecht-Karls-Universität Heidelberg

Medizinische Fakultät Mannheim

Dissertations-Kurzfassung

Striatal Reward Sensitivity as a Neurobiological Marker in Alcohol Use Disorder

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Translational models in clinical neuroscience propose the integrated study of neurobiological mechanisms and behavioral factors (e.g. symptoms, therapy outcome) to inform diagnosis and therapeutic interventions. *Alcohol use disorder* (AUD), as defined by the Diagnostic and Statistical Manual of the American Psychiatric Association, 5th edition (DSM-5), is a heterogeneous mental disorder. Multiple factors including biological and environmental aspects, as well as comorbidities like depression contribute to individual risk profiles which constitute distinct AUD phenotypes. Despite an advanced understanding of the neurobiological mechanisms underlying AUD, psychotherapeutic interventions are still modestly effective in preventing relapse. However, neuroimaging research now allows the characterization of subtypes based on dimensions of neural alterations. Therefore, one aim of translational neuroscience is to increase treatment efficacy through the identification of brain-based biomarkers. Considerable evidence proposes that the onset and maintenance of AUD is associated with dysfunctional reward processing, specifically altered incentive salience or "wanting". Mediated primarily by the *ventral striatum* (VS), incentive salience drives goal-directed behavior by motivating approach towards rewards. Considerable evidence highlights the role of the VS for the hazardous "wanting" of alcohol. However, individual differences in the "wanting" of conventional, non-drug rewards (e.g. money) have also been identified as a potential risk factor in AUD. By using a reliable monetary reward paradigm, we were interested in investigating whether VS sensitivity to reward might represent a promising candidate biomarker which may be used to help inform diagnosis and therapeutic options for AUD. The results of the first study of this dissertation provide evidence that AUD is characterized by an imbalance between increased VS activation and weakened prefrontal control, as characterized by decreased frontostriatal connectivity during the anticipation of monetary reward. Moreover, we demonstrated that increased VS activation and decreased frontostriatal connectivity were associated with increased craving, further supporting the functional relevance of the identified brain mechanisms for AUD. Based on the results of the first empirical study, we were interested on whether VS reward sensitivity may be able to serve as a neurobiological marker for predicting responsiveness to therapy. We investigated this question in a clinical intervention study using *cue exposure training* (CET) as the intervention in question in comparison to *treatment as usual* (TAU). CET has been introduced as a psychotherapeutic intervention gradually targeting the extinction of conditioned alcohol-associated responses through repeated unreinforced exposure. The results of the second study of this dissertation revealed that following CET therapy those patients with increased VS reward sensitivity showed a more positive signal change in the superior frontal gyrus and anterior cingulate cortex. Again, all AUD patients showed that self-efficacy to abstain was related to a stronger signal change in the identified *prefrontal cortex* (PFC) brain regions, specifically the superior frontal gyrus and anterior cingulate cortex. In line with our results of the first study, these findings highlight the role of the PFC and frontostriatal network as affected target networks relevant for behavior change in AUD. Furthermore, both empirical findings provide evidence that VS reward sensitivity might be a promising candidate for a neurobiological marker that could be applied in the context of personalized therapy. Finally based on recent advances in the field and our own work, a mechanism of striatal reward sensitivity is proposed. The proposed mechanism aims at providing a conceptual framework of distinct neurobiological subtypes in AUD that is translatable into psychotherapeutic interventions. According to the proposed mechanism, either an excess (hyperactive subtype) or a deficit (hypoactive subtype) in incentive salience regulation of the VS, modulated by impaired PFC functioning, can result in self-regulation failure and ultimately result in relapse. According to the individual risk profiles, potential psychotherapeutic treatment options are reviewed. While the model is preliminary in nature, it may offer a foundation to inform future transdiagnostic and personalized research.