Summary

Decoding Conduct Disorder: A Multi-Method Approach using Computational Modeling, fMRI and Machine Learning – M.Sc. Erik M. Elster

Introduction

Conduct Disorder (CD) is a complex and multifaceted psychiatric condition marked by persistent patterns of antisocial behavior, often accompanied by aggression and violations of social norms (American Psychiatric Association, 2013). Affecting approximately 2-3% of school-aged children globally, CD has profound implications for individual functioning and societal costs (Polanczyk et al., 2015). Despite its high prevalence, the underlying neurocognitive and neural mechanisms remain poorly understood. This dissertation employs a multi-method approach to address these gaps, integrating computational modeling, functional magnetic resonance imaging (fMRI), and machine learning (ML). The overarching goal is to elucidate the cognitive and neural processes underlying CD, with a specific focus on the roles of callous-unemotional (CU) traits and sex differences in shaping its behavioral and neurobiological profiles.

Study 1: Impaired Punishment Learning in Conduct Disorder

The first study investigates reinforcement learning (RL) deficits in individuals with CD by utilizing a probabilistic RL task (Baumann et al., 2022). The aim of the study was to examine whether individuals with CD in their capacity to learning from punishment and reward compared to typically developing controls (TDCs) (Byrd et al., 2014, 2018). Participants completed a task designed to measure their ability to associate stimuli with positive (reward) or negative (punishment) outcomes. Computational modeling was applied utilizing the Rescorla-Wagner learning rule to extract learning parameters for all participants individually (Lockwood & Klein-Flügge, 2021; Rescorla & Wagner, 1972). The results revealed a significant difference in punishment learning among individuals with CD, indicating a diminished capacity to adjust behavior based on negative feedback. These findings support the ‘punishment insensitivity’ hypothesis in CD and underscore the importance of understanding RL mechanisms to address the behavioral challenges associated with the disorder.

Study 2: Altered Neural Punishment Learning in Conduct Disorder

Building on the behavioral findings, Study 2 investigates the neural correlates of reinforcement learning (RL) deficits in individuals with CD. This study employs model-based fMRI by incorporating Prediction Errors (PEs) as parametric modulators, which were calculated using the individual learning parameters derived from Study 1. Linear regression analyses were conducted to evaluate the relationship between learning parameters and neural activity across key brain regions. The results revealed a significant finding in the anterior insula, where individuals with CD showed altered neural responses to punishment. This suggests that the anterior insula plays a critical role in punishment learning and that its dysfunction in CD may contribute to deficits in behavioral adaptation to negative outcomes (Fairchild et al., 2019). However, no significant differences were observed in other brain regions typically implicated in RL, such as the ventral striatum (VS), ventromedial prefrontal cortex/orbitofrontal cortex (vmPFC/OFC), the amygdala, and the anterior cingulate cortex (ACC). These findings underscore the anterior insula's central role in CD-related deficits in punishment learning.

Study 3: Machine Learning Reveals Sex Differences in Distinguishing Between Conduct-Disordered and Neurotypical Youth Based on Emotion Processing Dysfunction

With CD being more prevalent in boys than in girls, the third study aimed to investigate sex differences through the lens of the 'differential threshold' hypothesis. This hypothesis posits that girls with CD exhibit more pronounced emotion dysfunction than boys to meet the threshold for similar behavioral manifestations. To explore this, the study employed machine learning (ML) techniques to identify sex-specific neurocognitive markers of CD. Using the Generalized Matrix Learning Vector Quantization (Angle-GMLVQ) classifier, the study achieved classification of CD based on neurocognitive features of emotion processing above chance level, though still below clinically relevant accuracy.

Further, the findings reveal distinct patterns of emotion processing deficits between boys and girls with CD. Girls displayed significant impairments in recognizing positive emotions, such as happiness, which may contribute to relational aggression and

difficulties in forming positive social connections. In contrast, boys exhibited deficits in recognizing fear, potentially aligning with their higher rates of overt aggression and risk-taking behaviors (Konrad et al., 2022; Smaragdi et al., 2017). This study highlights the heterogeneous nature of CD and provides new insights into emotional processing mechanisms that differentiate boys and girls with the disorder.

Discussion and Implications

The dissertation synthesizes findings across the three studies, emphasizing the interplay between behavioral, neural, and sex-specific factors in shaping CD. By integrating advanced methodologies, this research provides a comprehensive framework for understanding the heterogeneity of CD and highlights the importance of individualized diagnostic and potentially therapeutic strategies. Further, the findings advocate for the use of computational modeling, model-based fMRI, and ML as powerful tools in psychiatry, capable of uncovering subtle patterns and mechanisms that traditional approaches may overlook.

Future research should focus on longitudinal studies to track the developmental trajectories of RL deficits and neural dysfunctions in CD, as well as investigate the efficacy of targeted interventions informed by these findings. By addressing the heterogeneity of CD, this dissertation lays the groundwork for a more nuanced and personalized approach to understanding and treating CD.

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